ABSTRACTS OF WORLD MEDICINE

VOL. 17 NO. 1 JANUARY, 1955

Pathology

EXPERIMENTAL PATHOLOGY

1. **Mechanisms of Wound Healing. Comparison of Preliminary Local and Distant Incisions**
E. D. SAVLOV and J. E. DUNPHY. *New England Journal of Medicine* [*New Engl. J. Med.*] **250**, 1062–1065, June 24, 1954. 2 figs., 8 refs.

A preliminary analysis of the role of systemic and local factors in the process of wound healing is reported in this paper from the Peter Bent Brigham Hospital (Harvard Medical School). In a number of anaesthetized Hisaw rats the tensile strength of healing abdominal incisions was determined by attaching one side of the wound to a fixed pole and the opposite side to a plastic bag suspended over a pulley. Increasing tension on the wound was produced by a steady flow of water into the bag. The weight of the bag and the water at the time of complete separation of the abdominal wall was taken as the disruption strength.

No greater tensile strength was observed on the third day in wounds of the abdomen made 15 days after incisions on the back than in 3-day-old abdominal lesions in a control group of animals not previously wounded. When, however, 15-day-old abdominal wounds were opened and resutured a significant increase in tensile strength was observed on the third day after resuture. *A. Wynn Williams*

2. **Experimental Studies Concerning Factors in the Pathogenesis of Acute Pancreatitis**
M. A. BLOCK, K. G. WAKIM, and A. H. BAGGENSTOSS. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **99**, 83–90, July, 1954. 5 figs., 13 refs.

An attempt was made at the Mayo Clinic to produce in rats pancreatic lesions similar to those observed in pancreatitis in human beings. Partial or complete obstruction of the common bile duct below the entrance of the pancreatic ducts caused pancreatic oedema, lymphocytic infiltration, fat necrosis of the tissues around the pancreas, and dilatation of the ducts and acini. The lesions were similar to those seen in acute pancreatic oedema. When the common bile duct was ligated above as well as below the entrance of the pancreatic ducts the same changes were observed, lending support to the view that, in the rat at least, biliary reflux into the pancreas is not a factor in the production of these changes.

By ligation of the greater part of the pancreatic blood supply parenchymal necrosis was produced and, occasionally, fat necrosis. When ligation of the common bile duct was combined with occlusion of pancreatic vessels a condition closely resembling acute haemorrhagic pancreatitis in man was observed. The authors believe that the clinical features of acute pancreatic oedema are the result of obstruction of the pancreatic duct, and that when vascular thrombosis occurs, acute haemorrhagic pancreatitis develops. *A. C. Parks*

CHEMICAL PATHOLOGY

3. **The Effect of the Cerebrospinal Fluid on the Crystallization of Cupric Chloride in Cases of Tuberculous Meningitis.** (Über die Beeinflussbarkeit der Kupferchlorid-Kristallisation durch Liquor cerebrospinalis bei Meningitis tuberculosa)
F. LEHMANN-GRUBE. *Archiv für Psychiatrie und Nervenkrankheiten* [*Arch. Psychiat. Nervenkr.*] **192**, 207–219, 1954. 8 figs., 13 refs.

It was reported by Tomesco in 1936 that the crystallization of chlorides from physiological saline to which cerebrospinal fluid (C.S.F.) had been added in various proportions and which had then been allowed to evaporate was modified under pathological conditions, giving rise to recognizable changes in the gross and microscopic appearance of the crystals. He considered this to be due to the influence of an excess of proteins on the surface of the drop of C.S.F. A similar effect on the crystallization of copper salts was reported by Riebeling in 1952, and the present author has applied Riebeling's technique to the examination of the C.S.F. in cases of tuberculous meningitis treated at the Hamburg General Hospital and Neurological Clinic. The technique is described as follows. Into a clean test tube 0·1 ml. of C.S.F. (not blood-stained) is measured. After centrifuging for 10 minutes at 2,500 r.p.m., 0·15 ml. of acidified cupric chloride solution is added, the copper solution being prepared by dissolving 25 g. of pure $CuCl_2$ in 75 ml. of water and adding 50 ml. of N/10 hydrochloric acid. A few drops of the mixture are then placed on a clean slide and left in a dust-free place to allow crystallization to occur. The findings of Riebeling that characteristic crystallization forms are obtained with normal C.S.F. and that those obtained with pathological C.S.F. are entirely different were confirmed, and the patterns formed by the crystals, which resemble grasses in blossom, are described and illustrated by photomicrographs. The results of examination of 124 specimens of C.S.F. from 59 cases of tuberculous

meningitis are divided into three groups. (1) Where the standard tests gave markedly pathological findings the characteristic crystallization forms appeared regularly. (2) Where the other findings were only slightly abnormal the result of the crystallization test was strongly positive in 13 out of 30 cases and suggestive of organic disease in 7 others. (3) The C.S.F. from convalescent patients gave positive results in a few cases.

Since in many cases a positive result is obtained when the protein content of the C.S.F. is not increased, and since the cellular elements are removed for the purposes of the test, the author concludes that the modification of crystallization must be due to some abnormal factor not detectable by the usual methods of investigation of C.S.F. *E. Forrai*

4. Survey of Clinical Significance of Serum Mucoprotein Level

E. M. GREENSPAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **93**, 863–874, June, 1954. 1 fig., 14 refs.

Serum mucoprotein determinations were carried out on blood taken from 1,533 patients with various diseases on admission to hospital, and the results correlated with the clinical condition. The normal range was taken as 40 to 70 mg. per 100 ml. for females and 48 to 75 mg. per 100 ml. for males.

Of 52 cases of acute infectious diseases such as pneumonia, enteritis, and cellulitis, but excluding infectious mononucleosis and infective hepatitis, the serum mucoprotein level was raised in all. Of 14 cases of infectious mononucleosis, only in 7 was the level raised, while in one case a reduced value was found; all these patients had either hepatomegaly or jaundice. Of 123 patients with subacute or chronic inflammatory diseases (excluding involvement of the liver or biliary tract), the level was raised in 87 and reduced in 3, 2 of whom had ulcerative colitis with evidence of severe parenchymatous disease of the liver.

Of 33 cases of benign neoplasm, the serum mucoprotein level was above normal in 1 and depressed in 6. However, raised values occurred in 218 out of a total of 298 cases of malignant neoplasm, although those patients with primary cancer of the head or neck, with or without metastasis, showed a raised value in only about 50% of cases, while a subnormal value occurred in 7 out of 11 cases of multiple myeloma.

Very few low serum mucoprotein values were found among patients with cardiovascular, renal, collagen, or rheumatic diseases, the level being above normal in 120 out of 193 cases in this category. Increased values occurred in 16 out of 18 patients with rheumatoid arthritis and in 15 out of 17 patients with active rheumatic fever. In contrast, only in 10 out of 20 cases of disseminated lupus erythematosus (all with arthritic manifestations) were raised values found. In general, the level was low in patients with the nephrotic syndrome and high in those with glomerulonephritis or nephrosclerosis with uraemia.

Metabolic and endocrine diseases were characterized by normal or low serum mucoprotein levels, only 19 out of 214 patients having a high level compared with 61 with a low level. In particular, low values were found in panhypopituitarism (5 out of 7 cases) and Addison's disease (8 out of 11 cases). Only in one out of 9 cases of pernicious anaemia was the level low. Evidence was obtained that serum mucoprotein determinations may be of value in differentiating hepatogenous from obstructive jaundice. Of 177 cases of primary parenchymatous hepatic disease, the level was low in 138, while of 137 patients with obstructive biliary disease, a low value was found in only 4. Low values were uncommon in patients with hepatomegaly due to congestive heart failure (3 out of 30), lymphoma or leukaemia (one out of 46), or metastatic disease (*nil* out of 63).

The author presents the hypothesis that the serum mucoprotein level at any one time represents an equilibrium between hepatic and endocrine factors, tending to reduce it, and inflammatory and tissue proliferative processes tending to increase it. *M. Lubran*

5. Behavior of Serum Iron in Various Diseases of Liver

E. R. CHRISTIAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 22–33, July, 1954. 10 refs.

The serum iron level in various diseases of the liver and its value in the differential diagnosis of hepatic disease, particularly that associated with jaundice, are discussed. At the Veterans Administration Hospital, New Orleans, and Tulane University of Louisiana the iron content of serum showing no visible haemolysis from 313 subjects was determined according to the method of Schales, the total number of estimations being 659. Of the 313 subjects, 50 were healthy; 15 were considered to be healthy originally, but were later excluded from the group of healthy subjects because of abnormal response to liver function tests; 28 were hospital patients without liver disease; 27 had liver disease due to undetermined causes; and 193 had liver disease the exact nature of which was established by needle biopsy or at laparotomy or necropsy (viral hepatitis 33, granulomatous hepatitis 15, other hepatitis 31, portal cirrhosis 23, necrotizing phase of portal cirrhosis 11, fatty metamorphosis 24, extrahepatic biliary obstruction 14, neoplastic disease of the liver 10, passive congestion of the liver 12, haemochromatosis 3, and liver siderosis other than haemochromatosis, 17). Values for total bilirubin, thymol turbidity, gamma globulin, lipid turbidity, and cephalin flocculation were determined for all specimens of serum, and cholesterol partition tests were carried out on selected specimens. Additional laboratory investigations in the patients with liver disease included estimation of serum total protein, albumin : globulin ratio, and prothrombin time, and the urobilinogen content of urine and faeces; the "bromsulphalein" retention test was also carried out in this group.

It was found that hepatocellular damage raised the serum iron level above normal (about 143 μg. per 100 ml.), the rise usually being higher in viral hepatitis than in any other of the liver diseases studied except haemochromatosis. In viral hepatitis the serum iron level roughly paralleled the clinical course of the disease; there was,

however, no constant correlation between this level and the severity of the disease or the results of other liver function tests. It is suggested that in liver disease with jaundice (unless jaundice is due to haemolysis) a serum iron level above 300 μg. per 100 ml. is diagnostic of viral hepatitis. However, a significant increase in the serum iron level is sometimes observed in various types of hepatitis and in the necrotizing phase of portal cirrhosis, the increase being roughly proportional to the extent of hepatocellular damage. The author considers that the serum iron level is of value in differentiating viral hepatitis from extrahepatic biliary obstruction, particularly when obstructive phenomena are present in hepatitis. Further, estimation of the serum iron level should be used as an adjuvant to other liver function tests and liver biopsy in the investigation of cases of hepatocellular damage, although in some cases it is more specific than either liver function tests or liver biopsy. *J. E. Page*

6. Serum Phosphorus and Potassium Levels after Intravenous Administration of Glucose. Their Use as Diagnostic Aids in Diabetic and Nondiabetic Subjects with and without Liver Disease

K. GUNDERSEN, R. F. BRADLEY, and A. MARBLE. *New England Journal of Medicine* [*New Engl. J. Med.*] **250**, 547–554, April 1, 1954. 31 refs.

Serum potassium and inorganic phosphorus levels were estimated during the course of glucose tolerance tests in 11 healthy subjects and 41 patients at the New England Deaconess Hospital, Boston, the object being to determine if the fall in the serum concentrations of phosphorus and potassium during intravenous infusion of glucose was of value in the diagnosis of diabetes mellitus. Since it has been suggested that the hyperglycaemia of elderly diabetic patients may be due to liver dysfunction, the possible presence of liver disease was determined from the patient's past history, observation of gross hepatic enlargement, and the results of laboratory investigations, which included estimation of serum bilirubin and protein levels and the thymol turbidity test. The glucose tolerance curve was considered to be normal if the fasting blood glucose level was 100 mg. per 100 ml. or less, and if the blood sugar concentration returned to the fasting level within 2 hours.

In 24 of the subjects in whom the glucose tolerance curve was normal the maximum fall in the serum phosphorus level averaged 19% (range 4 to 35%); in 4 in whom the glucose tolerance curve was equivocal the average fall was 22% (range 13 to 29%); and in the remaining 24 diabetic patients in whom the curve was abnormal the average fall was 18% (range 5 to 35%). Liver function was normal in 26 subjects, the glucose tolerance curve being normal in 17, equivocal in 2, and diabetic in 7; the maximum fall in the serum phosphorus level in this group averaged 19·8%. Of 5 patients with definite liver disease the glucose tolerance curve was abnormal in 4; the maximum fall in the serum phosphorus level in this group averaged 15·8%. In the remaining 21 patients there was suggestive evidence of liver disease, 6 having hepatomegaly and 15 showing minor abnormalities in their response to liver function tests; the average fall in the serum phosphorus level in these two groups was 16·1% and 19·4% respectively. The decrease in the serum potassium concentration averaged 0·33 mEq. per litre when the glucose tolerance curve was normal and 0·32 mEq. per litre when it was abnormal.

The authors conclude that the maximum fall in the serum phosphorus level and the decrease in the serum potassium concentration during an intravenous glucose tolerance test cannot be relied upon to differentiate true diabetes mellitus from so-called hepatic storage insufficiency or to determine the presence of slight degrees of insulin deficiency. *M. J. H. Smith*

7. Some Studies of Nature and Clinical Significance of Porphobilinogen

C. J. WATSON. *Archives of Internal Medicine* [*Arch. intern. Med.*] **93**, 643–657, May, 1954. 2 figs., 24 refs.

Crystalline porphobilinogen is partially converted by heat at *p*H 3·5 or less to a uroporphyrin-type porphyrin. However, some solutions of impure porphobilinogen are not so converted until the *p*H is as acid as 0·8 or 0·7. Normal urine markedly depresses porphyrin formation from crystalline porphobilinogen, but urea, sodium chloride, and creatinine are without effect. Uric acid, however, produces a marked depression of porphyrin production, and as a considerable amount of uric acid is present in crude porphobilinogen solutions, their anomalous behaviour may be due to the formation of a porphobilinogen–uric-acid complex. The porphyrins isolated from the urine in acute porphyria are not identical with the uroporphyrins made by heating porphobilinogen and the coproporphyrin mixture obtained from it. It is suggested that the conversion of porphobilinogen to porphyrin *in vivo* may differ significantly from that resulting from heating *in vitro*.

The insolubility in chloroform of the Ehrlich aldehyde compound of urinary porphobilinogen is a useful screening test for acute porphyria, only 11 false positive reactions having been found by the author in thousands of tests, but it is recommended that specimens giving a faint orange or pink reaction in the chloroform-insoluble fraction should be disregarded unless they show an absorption band at 560 to 565 mμ. When the urine is rich in urobilinogen there may be a small fraction of aldehyde colour unextractable with chloroform, in which case the urine should be diluted 1 in 5, acidified with acetic acid, and extracted three times with ethyl acetate, when any positive reaction will definitely be due to porphobilinogen. Small amounts of porphobilinogen at times accompany large amounts of urobilinogen, especially in liver disease. As porphobilinogenuria without increased porphyrin production may occur only for brief periods in acute porphyria, the urine should be examined at the height of the attacks in any case of unexplained abdominal pain or acute or subacute neuropathy in which acute porphyria is suspected.

Only a rough quantitative estimation of porphobilinogen in urine is possible at present, the colour intensity obtained with a known amount in alkaline

solution depending partly on the type of Ehrlich reagent added and partly on other factors as yet unknown. Beer's law is obeyed, at least up to a concentration of 1 mg. of porphobilinogen per 100 ml.; at this concentration the Ehrlich aldehyde colour is equivalent to that given by 0·4 to 2·1 mg. of urobilinogen per 100 ml. In acute porphyria, values between 2 and 20 mg. per 100 ml. are obtained. A convenient semi-quantitative method using the Vahlquist type of Ehrlich reagent (*Hoppe-Seyl. Z. physiol. Chem.*, 1939, **259**, 213) is described in which 5 ml. of urine is treated with 5 ml. of Ehrlich reagent and 10 ml. of saturated sodium acetate solution, filtered, and read in an Evelyn colorimeter with the 550 filter after a few minutes. For the blank, the sodium acetate is added first, then the Ehrlich reagent, and the reading made at once, after filtration. The concentration is read from a calibration curve drawn on semilog. paper. [The curve is a straight line. With the final concentration of porphobilinogen in mg. per 100 ml. as the abscissa and the galvanometer reading as the ordinate (log-scale), the line passes through the points (0, 10) and (0·12, 4).] *M. Lubran*

8. **Evaluation of Occult-blood Tests on Faeces**
J. W. B. Forshaw and G. M. Mason. *Lancet* [*Lancet*] **2**, 470–473, Sept. 4, 1954. 13 figs.

In a study carried out at Liverpool Stanley Hospital the authors have compared the results of the amidopyrine, guaiacum, benzidine, and Gregersen tests for occult blood in faeces, with special reference to relative sensitivity, the influence of diet, and the effects of medicinal iron. Estimation of the sensitivity of the tests *in vitro* by testing serial dilutions of blood in water showed that the Gregersen test was the most sensitive, followed in order by the amidopyrine, benzidine, and guaiacum tests. They then determined the amount of blood which, when taken by mouth, produced a positive occult-blood reaction in the faeces of 7 healthy young men. In no case did 5 ml. of blood produce a positive reaction with the Gregersen test, but this amount gave a positive result with the other three tests in 2 of the subjects. Increasing the amount of ingested blood to 8 to 10 ml. produced positive results with the benzidine and amidopyrine tests in all cases, in all but one with the guaiacum test, and in all but 2 with the Gregersen test; these negative results became positive when 13 ml. of blood was taken. The four tests were next carried out *in vitro* on three preparations of iron, namely, a 10% solution of ferrous sulphate, a 10% solution of ferric chloride, and a 25% solution of a ferric ammonium citrate mixture. None of these medicinal iron preparations gave a positive result with any of the tests.

Lastly, the tests were applied to the examination of 128 specimens of faeces from 13 male hospital patients who were not anaemic and in whom gastrointestinal bleeding could reasonably be expected to be absent. The patients were allowed to brush their teeth and received an ordinary diet; 95 of the specimens were obtained while the patients were being treated with medicinal iron. Of a total of 512 test results, 97 were positive, but 62 of these were obtained from faeces passed within 3 days of the consumption of liver or black pudding (a kind of sausage made from blood). When these latter results were omitted it was found that the amidopyrine test gave 91% of negative results, 8% of weakly positive results, and only 1% of positive results; for the benzidine test the corresponding figures were 91%, 6%, and 3%; for the Gregersen test 95%, 4%, and 1%; and for the guaiacum test 91%, 8%, and 1%. The authors conclude that the sensitivity of the four tests is very similar, that medicinal iron does not cause false positive reactions, and that dietary restriction (except for withholding black pudding, liver, and kidney) and the forbidding of brushing of the teeth are unnecessary.

[Most workers are in agreement with the conclusion that the Gregersen test is unaffected by a normal diet, but when the benzidine test is used dietary restriction, such as the exclusion of meat or green vegetables, is generally considered necessary, and the authors' results would need confirmation before this precaution is omitted.] *M. J. H. Smith*

HAEMATOLOGY

9. **A Study of the Blood Groups in Habitual Abortion**
C. McNeil, L. C. Warenski, C. D. Fullmer, and E. F. Trentelman. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 767–773, July, 1954. 25 refs.

At the Holy Cross Hospital (University of Utah College of Medicine), Salt Lake City, the ABO blood groups were determined in 404 married couples selected at random; in 85 of these the wife had suffered abortion 2 or more times before the twentieth week of gestation. A significant excess of ABO incompatible matings was found amongst these couples, whose serum also contained immune anti-A or anti-B antibodies more frequently than the remainder. In contrast, the lowest incidence of abortion was found where both husband and wife were of Group O.

From the findings in this series it is suggested ABO incompatibility between mother and foetus plays an important role in abortion. *I. Dunsford*

10. **The Antithrombin Activity of Human Plasma**
J. W. Lyttleton. *Biochemical Journal* [*Biochem. J.*] **58**, 8–15, 1954. 7 figs., 23 refs.

The author refers to the apparent differences in behaviour of human and bovine antithrombin which have been previously noted by various workers. In this paper he reports the results of investigations carried out at the Lister Institute of Preventive Medicine, London, of the antithrombin activity of human plasma in a variety of conditions. Samples of various preparations of defibrinated human plasma were incubated with a purified preparation of human thrombin in veronal buffer at 37° C. and the decay of thrombin activity was followed by coagulating a solution of bovine fibrinogen with samples removed at regular intervals.

The antithrombin action of the blood was found to be progressive, and to depend on the concentration of both

thrombin and antithrombin. It is suggested, therefore, that the measurement of antithrombin activity should be in terms of velocity of thrombin inactivation rather than of the number of units of thrombin inactivated. The antithrombin responsible for the progressive decay of thrombin occurs in the α-globulin fraction of both serum and plasma, and not in the albumin as previously supposed. Partial purification of antithrombin was achieved by ether fractionation of plasma and showed that the active fraction contained 30% of α globulin. The optimum temperature for antithrombin activity was between 35° and 40° C. *A. Brown*

11. **The Antithrombin Activity of Heparin**
J. W. LYTTLETON. *Biochemical Journal* [*Biochem. J.*] **58**, 15–23, 1954. 8 figs., 12 refs.

It has for many years been accepted that the anticoagulant action of heparin is twofold: its power to inhibit the conversion of prothrombin to thrombin—for which it requires a plasma co-factor—and its inhibition of the action of thrombin on fibrinogen. It is the latter action of heparin which was the subject of the present study here reported from the Lister Institute of Preventive Medicine, London.

When thrombin was incubated with varying concentrations of heparin it was found that the latter exerted two different effects: (1) a slow progressive inactivation of the thrombin preparation, which was predominant at low concentrations of heparin (between 0·073 and 0·66 unit per ml.); and (2) an immediate fall in thrombin activity, which was most marked with heparin concentrations above 1·0 unit per ml.

Further observations on the effects of varying concentrations of thrombin and heparin were in keeping with the view that the sudden fall in activity was due to the formation, by electrostatic attraction, of a reversible thrombin–heparin complex, which is less active than uncombined heparin. Observations on electrophoretic separation of two samples of thrombin lent support to this view. The author is unable to define the nature of the mechanism of progressive inactivation produced by lower concentrations of heparin. *A. Brown*

12. **Relationship of Certain Antihistamine Drugs to the Activation of Purified Prothrombin**
M. MURRAY, S. A. JOHNSON, and W. H. SEEGERS. *American Journal of Physiology* [*Amer. J. Physiol.*] **178**, 10–16, July, 1954. 2 figs., 23 refs.

The factors involved as components of plasma thromboplastin activity are calcium, Factor V, platelets, and a platelet co-factor. This paper from Wayne University College of Medicine, Detroit, describes the effect of substituting certain synthetic organic compounds for the platelet co-factor of plasma necessary for prothrombin conversion. A number of antihistamine substances, of which the chief were "linadryl" (4 : 2-benzhydryloxyethyl morpholine hydrochloride) and "benadryl" (diphenhydramine), were found to act as effective substitutes for the platelet co-factor under the conditions of the test. The authors believe that the platelet co-factor is similar to or identical with the antihaemophilic factor.

[No mention is made of Factor VII as a component of thromboplastin activity, nor of the action of the antihistamine drugs on haemophilic plasma.]

A. Brown

13. **Rouleaux Formation Intensity of Plasma and E.S.R.**
S. LEWI. *British Medical Journal* [*Brit. med. J.*] **2**, 336–338, Aug. 7, 1954. 2 figs., 14 refs.

In this paper from the National Blood Transfusion Centre, Paris, the author compares the results obtained with the Wintrobe and the Westergren methods of estimating the erythrocyte sedimentation rate in the presence of varying concentrations of the sedimenting factors, as judged by rouleaux formation and fibrinogen content, and varying concentrations of erythrocytes, as judged by the packed cell volume. He comes to the conclusion that the difference between the results obtained with diluted blood (Westergren method) and those obtained with undiluted blood (Wintrobe method) is essentially due to the simultaneous action of two effects of dilution—accelerating sedimentation by lowering the concentration of erythrocytes, and slowing it by diluting the plasma factors. When, however, the concentration of plasma factors is high in the presence of a normal concentration of erythrocytes a "zone phenomenon" sometimes masks the high sedimentation rate, and the Westergren method then gives better results by abolishing the phenomenon. For this reason, and because anaemia in an otherwise normal plasma does not cause such rapid sedimentation when the plasma is diluted, the author considers that the Westergren method gives values more closely correlated with the concentration of the abnormal plasma factors than does the Wintrobe method. *Marjorie Le Vay*

14. **The Determination of Blood Volume by the Polyvinylpyrrolidone Method.** (Détermination du volume sanguin par la méthode au polyvinyl-pyrolidone)
A. GOUTTAS, H. TSEVRENIS, H. YATZIDIS, and P. FESSAS. *Revue d'hématologie* [*Rev. Hémat.*] **9**, 180–188, 1954. 8 figs., 13 refs.

The authors of this paper from University Clinic B, Athens, review the methods available for the determination of blood volume and point out that each has some disadvantage. They themselves prefer the method first described by Piette and Poulain (*Bull. Soc. Chim. biol.* (*Paris*), 1948, **30**, 7) which employs polyvinylpyrrolidone (PVP), a substance of high molecular weight (25,000) which is water-soluble and devoid of toxicity even in high doses. Introduced intravenously, it is not fixed by the erythrocytes and is only slowly eliminated by the kidneys. They have modified the original technique in that they estimate the plasma concentration of PVP spectrophotometrically, the addition of iodine to solutions of PVP giving a stable, reddish-violet discoloration which can be detected in dilutions up to 1 in 100,000. A commercial preparation of PVP ("subtosan") is used, supplied in ampoules with a constant molecular concentration of 25%, 5 ml. being injected into an arm vein. Four minutes after the injection (6 minutes in patients with circulatory insufficiency) 5 ml.

of blood is taken from the other arm into a flask containing Wintrobe's anticoagulant. The erythrocyte volume is determined by means of the haematocrit, and the concentration of PVP in the plasma by spectrophotometry. [For details of the methods and calculations used the original paper should be consulted.]

This method is characterized by simplicity and rapidity, the results being obtainable in urgent cases within 20 minutes. The accuracy of the results was tested in 7 cases of exchange transfusion in which the amounts of blood removed and given were known exactly, the error being $\pm 2\%$. According to the authors' estimations the normal blood volume represents 7·95 to 8·55% of the body weight. They have also carried out estimations of blood volume in 90 cases of organic disease which may be divided into four groups. (1) In 22 cases of hepatic cirrhosis, with or without ascites, the volume was increased (without relation to oedema) and in 9 cases of infective hepatitis it was diminished; this last is stated to indicate a bad prognosis, especially if the fall is progressive. (2) In 9 cases of thyrotoxicosis there was no change, whereas in 7 cases of myxoedema there was a marked decrease. The blood volume of the latter was restored to normal after treatment with thyroid extract. (3) In 19 cases of gastric haemorrhage and 2 cases of ruptured extra-uterine pregnancy the blood volume was reduced to varying degrees, ranging from 45 to 57% of normal in those patients who died from haemorrhagic shock, the latter figure representing, in the authors' view, the lowest blood volume compatible with survival. (4) In a number of cases of hypertension no correlation was found between the blood volume and the degree of hypertension present. *E. Forrai*

15. **Leukoagglutinins. V. Leukoagglutinins in Chronic Idiopathic or Symptomatic Pancytopenia and in Paroxysmal Nocturnal Hemoglobinuria**
J. Dausset, A. Nenna, and H. Brecy. *Blood* [*Blood*] **9**, 696–720, July, 1954. 4 figs., bibliography.

The authors, working at the National Blood Transfusion Centre, Paris, have made a study of the leucocyte-agglutination phenomenon. Over 2,000 samples of serum have been examined, including 102 from patients with leucopenia. Among these latter, 19 have exhibited leucocyte agglutination, the phenomenon being consistently present in all the cases. The technique for obtaining leucocytes from normal donors is given, and the simple test used for detecting leuco-agglutinins is described. Causes of false positive reactions are pointed out and discussed.

All fresh sera were found to contain a thermolabile inhibitory substance, but it was noted that complement did not appear to be consumed in the reaction. The leuco-agglutination reaction involved both mononuclear cells and granulocytes, but certain primitive cells did not appear to be agglutinable. Heating at 65° C. for 30 minutes destroyed the leuco-agglutinin. Fractionation of the serum indicated that it is probably a gamma globulin. Pathologically affected leucocytes were not agglutinated by normal homologous serum, and specific anti-erythrocytic antibodies were found not to have any leucocyte-agglutinating properties. Serum containing leuco-agglutinin produced a profound leucopenia when injected into 2 patients.

The authors believe the phenomenon to be an immunological one, the leuco-agglutinin being an antibody of an undetermined type. All the patients in whose serum it was detected had previously received blood transfusions, which may have resulted in their sensitization. It has not been possible to produce agglutination by a pathological serum of its own leucocytes, although the profound leucopenia which was present in each case would suggest a relationship with leuco-agglutination and give support to a hypothesis of auto-immunization. The clinical material is described and analysed.

E. G. Rees

16. **Role of the Lungs in Regulation of the White Blood Cell Level**
C. M. Ambrus, J. L. Ambrus, G. C. Johnson, E. W. Packman, W. S. Chernick, N. Back, and J. W. E. Harrisson. *American Journal of Physiology* [*Amer. J. Physiol.*] **178**, 33–44, July, 1954. 11 figs., bibliography.

Previous observations by a number of workers have suggested that the pulmonary circulation may function as a leucocyte-filtering mechanism and thus act in maintaining a normal level of these cells in the blood. In the present paper from Jefferson Medical College, Philadelphia, experiments are described by which it was shown that leucocytes were rapidly removed from heparinized dog blood circulating in a canine heart–lung preparation until a level which appeared to be independent of the leucocyte content of the infused blood was reached. Similar results were obtained in experimental cross blood transfusion between intact donor dogs and heart–lung preparations in which no anticoagulants were used. When leucopenic blood was introduced into the preparation a gradual release of leucocytes from the lungs took place. In further experiments the filtering activity of the lungs was not influenced by the presence of " thorotrast ", an agent which powerfully inhibits the phagocytic activity of reticulo-endothelial elements.

The filtering activity of the lungs was shown to be very considerable and could not be exhausted during the useful life of the preparation employed, but the release of leucocytes appeared to be a small and more easily exhaustible process. Cardiac catheterization experiments provided confirmatory evidence of this leucocyte-filtering activity of the pulmonary circulation.

A. Brown

17. **A Morphological Sex Difference in the Polymorphonuclear Neutrophil Leucocytes**
W. M. Davidson and D. R. Smith. *British Medical Journal* [*Brit. med. J.*] **2**, 6–7, July 3, 1954. 7 figs., 6 refs.

A characteristic difference in morphology between the polymorphonuclear neutrophil leucocytes of males and females is described. In the female a solitary chromatin nodule 1·5 μ in diameter is to be found joined by a single filament to one lobe of the nucleus and having the shape of a drumstick. Other nuclear projections are described

and differentiated. In an examination of 375 blood films from female subjects the authors found such drumstick projections occurring with an average frequency of 1 in 38 cells, whereas none was seen in 500 neutrophils examined in each of 125 films of blood from males.

Marjorie Le Vay

18. **Bone Marrow**
J. M. YOFFEY. *British Medical Journal* [*Brit. med. J.*] **2**, 193–197, July 24, 1954. 1 fig., 37 refs.

A study at the University of Bristol of the various theories concerning lymphocyte production and destruction suggested that the bone marrow was a store or centre of destruction. A quantitative investigation of the lymphocytes in the bone marrow was therefore undertaken. Known weights of guinea-pig marrow were mixed with plasma in a mechanical shaker and the number of lymphocytes was estimated. It was found that the number of lymphocytes in the whole marrow was 30 to 60 times the number in the blood, and about equal to the daily thoracic duct output. Study of the myeloid series revealed a reserve in the marrow of about 100 times the number in the blood, and sufficient mature myeloid cells to raise the leucocyte count to 75,000 per c.mm. Similar estimation of the erythrocyte precursors indicated a much smaller margin of reserve.

Marjorie Le Vay

MORBID ANATOMY AND CYTOLOGY

19. **Atypical Proliferation of Bronchiolar Epithelium**
L. S. KING. *Archives of Pathology* [*Arch. Path. (Chicago)*] **58**, 59–70, July, 1954. 5 figs., 11 refs.

There have been a number of reports recently of the finding of peculiar small cellular proliferations in the lung, and opinions regarding the interpretation of these lesions have differed considerably. The author describes 15 cases, found in a series of 1,450 consecutive necropsies carried out at Illinois Masonic Hospital (University of Illinois), Chicago, which on routine histological examination showed foci of proliferation of epithelium of peculiar character in the distal portion of the bronchial tree. In none of the cases had this change been detected on gross examination.

In some cases the cell masses could be traced to the epithelium of small bronchi, bronchioles, and atria, but in others in which the cells filled up the alveoli a direct connexion to bronchiolar or atrial epithelium could not be demonstrated. The proliferations occurred immediately adjacent to areas of relative fixation of the lung which were due either to atelectasis, bronchiectasis, or fibrous tissue around a small artery, or to the immediate presence of an infarct or abscess. The cells were mostly of the spindle-shaped or oat-cell type in appearance and were usually very regular, although in some cases the main mass of proliferating cells showed varying amounts of squamous differentiation. The cells could be seen extending from one air sac to another, at first spreading along the margin and then filling the lumen; small masses were also present in spaces in the connective tissue.

The author considers that these atypical proliferations have two modes of development: (1) from the relatively undifferentiated cells that form the basal layer in the small bronchioles, and (2) from bronchial epithelium which has been stimulated by atelectasis and fibrosis to proliferate and line adjacent alveoli with cuboidal, spindle-shaped, or squamous cells, the last two types proliferating to form small solid clusters or masses of cells; the two types of growth may coexist. While these proliferations cannot be regarded as definitely non-neoplastic, it is the author's opinion that in the form in which they are most frequently observed " any malignant character would be only a possibility, not an actuality ".

A. Ackroyd

20. **The Histochemistry of Pulmonary Hyaline Membrane in Newborn Infants and its Interpretation**
J. C. WAGNER. *Lancet* [*Lancet*] **2**, 634–635, Sept. 25, 1954. 12 refs.

A histochemical investigation of the pulmonary hyaline membrane in newborn infants was undertaken at the South African Institute for Medical Research, Johannesburg. The lungs of 150 infants who died in the first week of life were examined, and in 41 pulmonary hyaline membrane was found. The membrane contained protein (positive Millon reaction) and was positive to periodic-acid–Schiff reagent (P.A.S.). It was not metachromatic, did not bind methylene blue below *p*H 4, and did not stain with alcian blue or Hale's colloidal iron. Acid mucopolysaccharides were therefore absent. P.A.S. staining was resistant to diastase, thus excluding glycogen, and to chloroform–methanol extraction, excluding lipids. The membrane therefore contained mucoprotein or glycoprotein. No lipid was found in frozen sections stained with Sudan black. Conventional stains showed no muscle or collagen (Masson's trichrome), fibrin (phosphotungstic-acid–haematoxylin), reticulin (Foot's silver), or elastic tissue (Verhoeff). In a case of tracheo-oesophageal fistula the membrane contained sudanophil lipids and fibrin.

Amniotic fluid obtained at Caesarean section was found to contain 0·6 g. of protein per 100 ml. The mucoprotein content was 80 mg. per 100 ml., and the polysaccharide content of the mucoprotein was 11 mg. per 100 ml. Mucoprotein, therefore, constitutes 13% of amniotic-fluid protein, compared with 1% in normal serum protein. In the author's opinion the mucoprotein content suggests that the hyaline membrane is formed from mucus of the upper respiratory tract.

M. C. Berenbaum

21. **Amyloid Neuropathy. A Clinical and Pathological Manifestation of Primary Atypical Amyloidosis with a Case Report.** [In English]
V. RITAMA and G. af BJÖRKESTEN. *Annales medicinae internae Fenniae* [*Ann. Med. intern. Fenn.*] **43**, 152–169, 1954. 10 figs., 19 refs.

In this paper from Helsinki a case is described in which the patient, a woman aged 54, had marked signs and symptoms of peripheral neuritis affecting particularly the lower limbs, but in which necropsy revealed

primary amyloidosis and pulmonary embolism. On histological examination numerous amyloid deposits were found in the peripheral nerves, including muscular and autonomic nerves. Deposits were also found in other sites, including the endocardium, smooth and skeletal muscle, and the endocrine glands.

The authors discuss the post-mortem findings in 19 cases of amyloidosis in adults, in 17 of which small deposits of amyloid were noted in the autonomic nerves. The " amyloid neuropathy " appeared to be more severe in those cases in which the parenchymatous organs were not infiltrated with amyloid. An inflammatory pathogenesis for the condition is suggested.

A. Wynn Williams

22. The Relationship between Muscle Damage and the Aschoff Cell in Rheumatic Carditis

B. RUEBNER. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 101–107, 1954. 4 figs., 24 refs.

The hearts of 32 patients dying of rheumatic carditis (of which 17 form the basis of this study) were examined at the University of Bristol in order to determine whether necrosis of muscle fibres occurs in rheumatic carditis and whether Aschoff bodies originate from damaged muscle cells or from connective-tissue cells—two questions which have been much disputed.

As a result of his study the author is led to the conclusion that the characteristic cells are not of muscular origin. He noted that there was a more intimate relationship between the Aschoff bodies and myocardial cells in cases with a brief clinical history. He concludes that the underlying lesion is a fibrinoid necrosis of the interstitial connective tissue which also involves the thin sarcolemma of the muscle fibres, and that this is sometimes accompanied by secondary damage to the muscle cells.

A. C. Lendrum

23. An Unusual Form of Alimentary Tract Ulceration in Infants

D. DEXTER and N. F. C. GOWING. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 259–269, 1954. 7 figs., 26 refs.

The authors present, from St. George's Hospital Medical School, London, 4 cases of infantile gastroenteritis in which certain unusual pathological features were found post mortem. The patients were aged between 3 and 11 months. In 3 of the cases diarrhoea appeared only after admission to hospital; in all 4 cases the disease progressed relentlessly in spite of chemotherapeutic and parenteral fluid therapy, and death occurred after 17 to 28 days. No pathogenic organisms or atypical strains of *Bacterium coli* were isolated from the faeces.

The most striking feature post mortem was the finding in the alimentary tract of apparently shallow ulcers up to 1 cm. in diameter with a yellow base and a surrounding zone of hyperaemia. In some cases, however, the necrosis had penetrated through the submucosa to deep in the muscle layers, and around some of the larger ulcers severe haemorrhage had occurred. The ulcers were found in the colon in all 4 cases, on the tongue in 3 cases, and in the terminal ileum, fauces, and vermiform appendix in one case each. Histologically, the lesions consisted of patches of coagulation necrosis of varying depth. Two notable findings were the presence of abundant, amorphous, basophilic, homogeneous material throughout the lesion and the absence of any inflammatory reaction. Necrotic cells and muscle fibres were embedded in the basophilic substance, and moderate numbers of mononuclear cells were seen in and around the lesions, accompanied by oedema, hyperaemia, and occasionally haemorrhage. There appeared to be an inverse relationship between the presence of the basophilic material and the degree of leucocytic infiltration.

No moniliae, fungi, or bacteria could be demonstrated in the lesions; at the periphery of some of the foci many cells had enlarged and vacuolated nuclei similar to those of cells attacked by the herpes simplex virus. In 2 cases vascular lesions occurred which were due to the accumulation of basophilic material in the lumen of small vessels. Because of its staining reactions the basophilic material was considered probably to be deoxyribonucleic acid. In discussing these cases the authors consider the possible relationship between the lesions and the antibiotic therapy (mainly aureomycin and chloramphenicol), but conclude that, though possible, such a causal relationship was not very likely since the lesions appeared in one case in which only a small quantity of penicillin was given. Bacterial or monilial infection was also ruled out by the negative bacteriological findings. The possibility of a virus infection appears most likely, and the authors report having been shown similar basophilic accumulations in a case of generalized infection with the virus of herpes simplex.

Ferdinand Hillman

24. Histochemistry of Whipple's Disease

W. G. B. CASSELMAN, A. I. MACRAE, and E. H. SIMMONS. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 67–84, 1954. Bibliography.

Writing from the University of Toronto, the authors describe the clinical, pathological, and histochemical features of 2 cases of intestinal lipodystrophy, the rare condition first described by Whipple in 1907. Both patients, a man of 38 and a woman of 62, died in Toronto General Hospital, and the definite diagnosis was made only post mortem. At necropsy the mesenteric lymph nodes were pale yellow and enlarged. In one case the jejunal mucosa was velvety and the mesenteric lymphatics dilated; in the other the intestinal appearances were normal. Histological findings characteristic of the disease were: (*a*) mononuclear cells with foamy, granular cytoplasm in the intestinal mucosa and mesenteric nodes; (*b*) dilated, lipid-filled lymphatics in the intestine, while in the mesenteric nodes the nodal structure was replaced by lipid-filled spaces; (*c*) hyaline, eosinophilic areas in the mesenteric nodes and (in one case) in the spleen, resembling amyloid but without its staining properties.

Histochemically, the mononuclear-cell granules contained a carbohydrate–protein complex. The carbohydrate was most probably a neutral mucopolysaccharide, as was shown by its staining properties, by its

giving a positive periodic-acid–Schiff reaction which was prevented by acetylation, by its resistance to hydrolysis by amylase, hyaluronidase, and pectinase, and by its failure to stain with methylene blue between *p*H 1·5 and 9·5. The presence of a protein moiety was confirmed by the xanthoprotein test, the Sakaguchi test for arginine, and the " coupled tetrazonium " reaction for tyrosine, tryptophane, and histidine. No lipid was demonstrated. The lipids in the dilated lymph spaces contained neutral fat and fatty acids (as shown by the Nile-blue test), cholesterol (Schultz test), phosphatides (Baker's acid haematin stain), and unsaturated lipids and their autoxidation products (positive performic-acid–Schiff reaction, prevented by bromination). Anisotropic crystals were present; some which melted at 65° to 70° C. were probably palmitic or stearic acid. A positive stain for calcium suggested the presence of calcium soaps.

The lymph-node lipids were extracted and analysed. It was found that lipids constituted 15% of their fresh weight, compared with 40% in control nodes. There was a relative increase in phosphatides and an absolute increase in cholesterol in the diseased nodes. [In the abstracter's opinion these results are largely invalidated by the fact that the tissues for histochemical study had been fixed in formaldehyde–saline solution for 10 days or longer.] The authors favour the theory that Whipple's disease is due to abnormal production of a polysaccharide–protein complex.

[Many other points are covered in the original paper, which should be read by those interested in this rare condition.] *M. C. Berenbaum*

25. **Renal Changes Including Total Cortical Necrosis in Cholera**

S. N. De, K. P. Sengupta, and N. N. Chanda. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **57**, 505–515, June, 1954. 6 figs., 37 refs.

In this paper from Nilratan Sircar Medical College, Calcutta, further work on the renal changes in cholera, based upon histological examination of the kidneys in 32 fatal cases of the disease, is reported. Of the 32 patients, 14 had died in the stage of shock, 10 in the stage of reaction, and 8 from post-choleric uraemia. Pickworth's stain was used to demonstrate the vascular pattern. In the first group there was some evidence in the kidneys of incomplete and patchy cortical ischaemia and of medullary congestion. Tubular cloudy swelling was present in the kidneys in some cases in the second group, but there was no cortical change or vascular disturbance. In the third group evidence of cortical ischaemia and medullary congestion was more marked than in the kidneys of patients who died in the stage of shock. Necrosis and fatty change of the cortical tubules and thickening and splitting of the glomerular basement membrane in the periodic-acid–Schiff preparations were constantly present. Selective damage to the upper or lower nephrons was not apparent. Some areas showed regenerative hyperplasia of tubular epithelium, and total necrosis was observed in some specimens. The pathogenesis of the condition is discussed. It appears that cholera regularly causes ischaemic damage to the renal cortex. Albuminuria and haematuria occur in mild cases, and obvious morphological changes, with the development of uraemia, in severe cases. The factors leading to severe ischaemia are obscure, but the presence of haemoglobinuria in 3 cases suggested that haemolysis may intensify vasospasm and thus increase the degree of ischaemia. *J. L. Markson*

26. **Needle Biopsy of the Liver: an Appraisal of its Diagnostic Indications and Limitations**

M. S. Kleckner. *Annals of Internal Medicine* [*Ann. intern. Med.*] **40**, 1177–1193, June, 1954. 3 figs., bibliography.

The diagnostic value and limitations of needle biopsy of the liver are discussed with reference to the histological findings in 145 consecutive cases in which needle biopsy of the liver was performed at the Northwestern University Medical School, Chicago. In all cases an adequate specimen of hepatic tissue was obtained by the Vim–Silverman or a modification of the Stauffer technique. Specimens were fixed in 10% formalin and stained with haematoxylin and eosin; a Berlin blue stain was used when haemochromatosis was suspected. The author describes the considerable diagnostic value of this procedure in many pathological conditions, including obscure hepatomegaly or jaundice, suspected cirrhosis, hepatitis, neoplasia, haemochromatosis, Banti's disease, or sarcoidosis, and even polycystic disease of the liver. Limitations of the method are the small size of the specimen and the " blind " procedure. In advanced cases of biliary, portal, or post-necrotic cirrhosis the histological appearances may be similar. Contra-indications include haemorrhagic tendencies, infection in or around the liver, and the presence of severe biliary stasis. There were 2 cases of bile peritonitis, one of which was fatal. *A. Wynn Williams*

27. **Differentiation of Megakaryocyte and Reed–Sternberg Cell, with Reference to the Periodic-acid–Schiff Reaction**

E. R. Fisher and J. B. Hazard. *Laboratory Investigation* [*Lab. Invest.*] **3**, 261–269, July–Aug., 1954. 3 figs., 12 refs.

The authors, writing from the Cleveland Clinic Foundation, Cleveland, Ohio, point out the difficulty of differentiating the Reed–Sternberg cells of Hodgkin's disease from megakaryocytes in tissue sections, and the consequent possibility of confusion in diagnosis. They have therefore attempted to establish consistent, easily reproducible, tinctorial differences between the two types of cell. Histochemical examination was made of 35 specimens of bone marrow and of 45 lymph nodes showing Hodgkin's disease (40 of the granuloma type), as well as a small number of specimens showing myeloid leukaemia, myeloid metaplasia, and Hodgkin's disease involving the stomach and bone marrow. The tissues were fixed in Zenker's acetic fluid for 6 to 16 hours, or in formalin.

A consistent difference was found between the two cell types with periodic-acid–Schiff staining. Whereas the Reed–Sternberg cell remained unstained or showed only slight blue-grey staining of a cytocentric zone

probably associated with the Golgi substance, the megakaryocyte cytoplasm stained an intense purple-red colour throughout. The staining of the megakaryocytes was resistant to diastase and was thus not due to glycogen. No lipids could be shown by staining with Sudan IV or oil red O. The result of staining for acid mucopolysaccharides with colloidal iron was inconclusive. The presence of a protein was shown by the positive results obtained with the Millon and " coupled diazonium " reactions. On these grounds the authors conclude that megakaryocytes contain a glycoprotein or mucoprotein. It is suggested that the difference in staining provides a simple method for the differentiation of these two types of cell.

[The authors' failure to demonstrate lipids in megakaryocytes must be attributed to their inadequate staining technique. Lipid is in fact present, and may be stained with Sudan black, as shown by Hayhoe (*J. Path. Bact.*, 1953, **65**, 413).] *M. C. Berenbaum*

28. **The Diffuse Vascular Lesion of so-called " Thrombotic Thrombocytopenic Purpura "**
H. W. MARCH. *Circulation* [*Circulation (N.Y.)*] **10**, 43–55, July, 1954. 6 figs., bibliography.

The literature on " thrombotic thrombocytopenic purpura " is reviewed and the gradual change in views on the aetiology of the disease is discussed in detail. The condition, when first described by Moschowitz in 1925, was believed to be primarily a disease of the platelets because of the characteristic features of purpura, haemolytic anaemia, and " platelet thrombi ". More recently many workers have suggested that it is a primary vascular disease of the collagen group, similar to polyarteritis nodosa and disseminated lupus erythematosus.

The present author develops the argument for this theory and describes one case in detail. Examination of the " thrombi " in the small vessels showed that they arose from a degeneration of the wall of the vessel and were not composed of platelets. The author discusses the aetiology, with special reference to an allergic or other immunological basis. He uses the term " thrombocytopenic verrucal angionecrosis ", and suggests that, as in some of the other collagen diseases, an abnormal immunological mechanism may be demonstrated when cases are recognized earlier enough for appropriate investigations to be carried out. *R. F. Jennison*

29. **Studies on Tumor Cells in Serous Effusion**
F. TAKAGI. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **24**, 663–675, June, 1954. 15 figs., 33 refs.

A study of 183 specimens of serous effusion from 136 patients with histologically proven neoplasms is reported from Washington University School of Medicine, St. Louis. The histological pattern of the neoplasm was generally reflected in the tumour cells found. The only reliable indications of malignancy were found to be the presence of: (1) clusters of cells of malignant appearance with an organoid arrangement; (2) individual cells with obvious malignant characteristics; and (3) cells staining positively for mucin. Cases of undifferentiated carcinoma arising in glandular tissue were found very difficult to diagnose, while atypical mesothelial cells occurring in effusions of long standing arising from such conditions as hepatic cirrhosis, cardiovascular disease, and sterile pleurisy gave rise to some difficulty. A positive diagnosis was made in a high proportion of cases of carcinoma of the stomach, breast, and ovary.
G. Calcutt

30. **Histogenesis and Biologic Behavior of Gastric Carcinoma. Study of One Hundred Thirty-eight Cases**
R. M. MULLIGAN and R. R. REMBER. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **58**, 1–25, July, 1954. 26 figs., 44 refs.

From an analysis made at the University of Colorado School of Medicine, Denver, of 138 cases of carcinoma of the stomach on the basis of histological and histochemical examination of the primary tumour obtained either at necropsy or by partial or complete resection of the stomach and regional lymph nodes, the authors conclude that there are three major histological types of gastric carcinoma, each with a characteristic biological behaviour. These are described as follows.

(1) Mucus-cell carcinoma, which frequently grows as signet-ring cells with mucin production or as undifferentiated cells, and also, although rarely, as differentiated glandular structures. This type has a significantly high incidence of onset before the age of 40. The primary tumour appears as a relatively large, flat, diffusely infiltrating growth, and has a high incidence of extension and metastasis, the " lethality rate " being of the order of 98%.

(2) Pyloro-cardiac-gland-cell carcinoma, which forms well-differentiated glandular structures, has a significantly high incidence in males, and is localized preponderantly to the antrum and cardia. The primary tumour usually appears as a delimited, fungating, sometimes widely ulcerated growth. It has less tendency to extend and metastasize than the mucus-cell type, and has a lethality rate of about 75%.

(3) Intestinal-cell carcinoma, which has two growth patterns. Both may be seen in the same tumour or they may occur in double primary tumours, the one being of a well-differentiated glandular type, and the other mainly undifferentiated. There is a relatively higher incidence of this type in females and its onset is usually after the age of 40. It is localized most frequently to the gastric fundus, and there is a significant association with pernicious anaemia. The primary tumour appears as a polypoid, a fungating, or a relatively flat, nodular, delimited growth with little propensity for extension and metastasis; the lethality rate of this type is thus lower, being about 60%

Radical gastrectomy, with secondary resection of any local recurrence, is indicated in most cases of Types 2 and 3 but not in Type 1, the mucus-cell carcinoma. The similarity of the growth patterns of pyloro-cardiac-gland-cell carcinoma and of endometrial glands during the menstrual cycle suggests that hormones such as androgens or oestrogens may be of value in the treatment of recurrent and metastatic carcinoma of this type.
A. Ackroyd

Bacteriology

BACTERIA

31. The Virulence of Isoniazid Resistant Tubercle Bacilli, Recovered from Patients during Treatment
G. MEISSNER. *Diseases of the Chest* [*Dis. Chest*] **26**, 15–26, July, 1954. 10 refs.

Isoniazid-resistant tubercle bacilli isolated from the sputum of patients during treatment with this drug show varying loss of virulence for guinea-pigs. The author, who has carried out experiments in this field at the Institute for Experimental Biology and Medicine, Borstel, Holstein, Germany, judged virulence by the ability of the culture, injected into guinea-pigs, to produce macroscopic tuberculous lesions in the organs (the sum of the number of lesions observed in a defined set of organs giving a numerical value which was used as an index). A culture index, depending on the results of culture from the same defined set of organs of the guinea-pig, was also employed. Pure isoniazid-resistant strains when freshly isolated from patients under treatment with this drug had a lower virulence for guinea-pigs than cultures of pure isoniazid-sensitive strains. Using both these methods the author found that sensitive strains inducing severe tuberculosis in the guinea-pig had a macroscopic index of 10 or more and a culture index of 5 or more, whereas resistant strains producing only minimal lesions had values of less than 2 for both macroscopic and culture indices.

The author stresses the importance of ensuring that cultures so tested are not mixtures of sensitive and resistant strains, and suggests that the discordant results obtained by other workers in this field might well be due to this. *H. J. Bensted*

32. Detection of Small Numbers of Tubercle Bacilli in Diagnosis. The Lethal Action of Concentrating Agents
D. F. GRAY, B. L. CLARKE, and W. E. JOHNSTONE. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 991–1001, June, 1954. 10 refs.

Having found that when a culture of *Mycobacterium tuberculosis* H37Rv grown on "tween"–albumin medium was washed once in albumin-water its sensitivity to penicillin (and presumably to other agents) was no longer increased by residual tween, and that of the 5 strains tested, H37Rv was the most sensitive to sodium hydroxide, the authors, at Melbourne University, used washed tween–albumin cultures to determine the lethal effects of concentrating agents, both on the cultures themselves and on non-tuberculous sputum to which the culture had been added.

As judged from viable counts on both culture and sputum, the survival rate of tubercle bacilli treated with concentrating agents was low: with a final concentration of 2% of NaOH it was 1·5 to 12·8%; with 11·5% trisodium phosphate it was 12·5 to 15·3%; with 3% sulphuric acid it was 0·4 to 1·9%; with 2·5% oxalic acid 0·7 to 0·9%; and with 54·5% of Jungmann's reagent it was less than 0·1%. The presence of sputum or of other viable organisms seemed to have little effect on the survival rate of the tubercle bacilli. All concentrating agents delayed growth. Similar results as regards survival rate were obtained in experiments carried out to determine infectivity to guinea-pigs of concentrated tuberculous material.

The authors conclude that 2% caustic soda for 30 minutes and 11·5% trisodium phosphate for 18 to 24 hours are the least unsatisfactory concentrating agents tried. *C. L. Oakley*

33. Type-12 Streptococci Associated with Acute Haemorrhagic Nephritis
M. J. WILMERS, A. C. CUNLIFFE, and R. E. O. WILLIAMS. *Lancet* [*Lancet*] **2**, 17–18, July 3, 1954. 4 refs.

The authors isolated Type-12 streptococci (Group A) from nose and/or throat swabs in 28 out of 31 cases of acute glomerulonephritis, while strains of Group-A streptococci, none of which was of Type 12, were isolated from similar swabs from 19 patients with acute rheumatism or anaphylactoid purpura. The authors state that in surveys carried out by the Public Health Laboratory Service for England and Wales in 1952 and 1953 to determine the incidence of various types of streptococci a total of 1,380 strains of Group-A streptococci were isolated, but only 8·2% of these were of Type 12. The authors consider their findings to suggest that in Britain, as in the U.S.A., there is a close relationship between acute glomerulonephritis and infection with Type-12 streptococci. *Joyce Wright*

34. The Haemolytic Activities of *Vibrio cholerae* and Related Vibrios
S. N. DE, K. BHATTACHARYYA, and P. K. ROYCHANDHURY. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **67**, 117–127, 1954. 20 refs.

The haemolytic test performed under standardized conditions with goat or sheep erythrocytes has proved for many years to be a very useful tool in differentiating the El Tor vibrio from the freshly isolated *Vibrio cholerae*. There has been some evidence brought forward to show that the test is not infallible and that the erythrocytes of different animals do not always react in the same way, but there has been little information available about the use of human erythrocytes in the test. The present authors report the results of parallel tests of a number of strains of *V. cholerae*, El Tor, and some "non-agglutinating" vibrios against erythrocyte suspensions of human and sheep origin, carried out at the Nilratan Sircar Medical College, Calcutta.

Peptone-water cultures (using "difco neopeptone") of all the vibrios tested haemolysed suspensions of

human erythrocytes in the tube test, but sheep erythrocytes were not haemolysed by any strains of *V. cholerae*. When calcium-free peptone-water was used, human erythrocytes were not haemolysed by *V. cholerae*, the haemolytic power of this organism being apparently dependent on the presence of calcium in the substrate. The haemolysin, which was thermolabile and diffusible, was held up by the asbestos pad of a Seitz filter, and the authors suggest that this accounts for the fact that filtrates of stools bacteriologically positive for *V. cholerae* are non-haemolytic. Human plasma contains calcium in a concentration equivalent to about 6 mg. per 100 ml., which is sufficient for the haemolytic activity to manifest itself, and it is therefore suggested that the intravascular haemolysis seen in cholera is due to the diffusion into the blood stream of the haemolysin produced by *V. cholerae* in the intestine.

[The authors' observations would not appear to lessen the value of the standard Grieg haemolytic test in differentiating the true cholera vibrio from the El Tor vibrio as a routine test.] *H. J. Bensted*

35. *Proteus* Infections in Hospital

P. Story. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 55–62, 1954. 2 figs., 5 refs.

To determine whether the source of *Proteus vulgaris* infection in hospital patients was extraneous or autogenous and also to assess the pathogenic role of the organism, all strains of *Proteus vulgaris* isolated during routine culture of pathological material from patients at St. Bartholomew's Hospital, London, were examined. Altogether the organism was isolated from specimens from 505 patients, often more than once. Smears from the lesion or the spun urinary deposit were examined for the presence of pus cells, this being regarded as evidence of bacterial infection; the sensitivity of the strains to antibiotics was also determined. For evidence of intestinal infection rectal swabs from 227 patients were cultured, strains of *Proteus vulgaris* being found in 173 instances. The similarity or otherwise of the strains was tested by means of the Dienes phenomenon, in which serologically dissimilar strains when swarming on the same agar plate leave a line of demarcation between their swarming areas; this is not observed when the strains are serologically identical.

The results indicated that, while the pathogenicity of *Proteus vulgaris* is difficult to assess, there is evidence that it may obscure the presence of other organisms whose disease-producing role is better established. This does not apply in the case of urinary infections, in which contaminant organisms can be excluded with greater ease. With the exception of 6 strains from specimens taken from patients in a plastic-surgery ward, it was uncommon to isolate similar strains of the same organism from material from patients in the same ward. The strain of *Proteus* obtained from the intestine was, however, identical with that from the lesion in 83% of cases, which suggested that autogenous infection was more usual.

[These results are in accord with those obtained by other workers.] *John M. Talbot*

VIRUSES

36. Typing of Poliomyelitis Viruses by Complement Fixation

G. L. Le Bouvier, G. D. Laurence, E. M. Parfitt, M. G. Jennens, and A. P. Goffe. *Lancet* [*Lancet*] **2**, 531–532, Sept. 11, 1954. 1 fig., 6 refs.

Many viruses can be identified by complement-fixation reactions with known antisera. Working at the Central Virus Reference Laboratory, Colindale, London, the authors have shown that by the use of antigens consisting of the liquid medium used for the growth of poliomyelitis virus in suitable cells, previously heated at 60° C. for 20 minutes, complement fixation was obtained with hyperimmune monkey serum of the homologous type, and little or no fixation with sera of the heterologous type. The technique employed is described in full [but cannot be adequately summarized]. The actual test consisted in titration on "perspex" plates, using a series of dilutions of serum and different dilutions of antigen together with 2·5 units of complement arranged in a chessboard pattern on the plates. Most of the tests were carried out with antigens produced by the growth of the virus in cells from monkey kidney. Cells from monkey testis were much less satisfactory, but cultures of HeLa cells—that is, cells derived from an epidermoid carcinoma of the cervix uteri—provided excellent antigens.

In a large series of estimations, for which cultures containing virus derived from faeces or sewage were used, it was found possible not only to identify the presence of poliomyelitis virus but to determine its type. The results obtained by complement fixation were similar to those obtained in direct virus neutralization tests. It is of interest that liquids from cultures of a known cytopathogenic strain of Coxsackie virus failed to fix complement with poliomyelitis antisera, and that although Coxsackie virus was present together with poliomyelitis virus in 3 out of 9 samples of sewage, complement fixation was obtained with poliomyelitis serum of the homologous type. The advantages and the practical application of the method, which is regarded mainly as a supplementary one, are discussed.

R. Hare

37. Lyophilization of Poliomyelitis Virus. Heat Inactivation of Dry MEF Virus

L. M. Kraft and E. C. Pollard. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 306–309, June, 1954. 2 figs., 9 refs.

At Yale University Medical School baby-mouse-brain suspensions of MEF1 poliomyelitis virus were employed as seed material for suspension in various media. The suspensions were shell-frozen in 0·2-ml. amounts and dried *in vacuo* with a condenser in series immersed in "methyl cellusolve" and dry ice. After drying, the material was reconstituted in water or in 30% peptone solution. Survival was best (32%) when the virus was suspended in peptone or sodium thioglycollate solution,

kept cold while drying, and resuspended in water. Suspension of the virus in water and reconstitution in 30% peptone solution was rather less satisfactory, only 10% surviving. Other suspending media gave much poorer results.

When preparations of dried MEF1 virus were held at different temperatures for varying periods of time it was shown that at room temperature (20° to 30° C.) there is some inactivation after only 20 minutes. On the other hand some preparations of virus were still capable of producing infection after heating at 80° C. for 20 minutes. This suggests that there are wide variations in ability of the virus suspension to resist heat. *R. Hare*

38. **Morphology of Type II Poliomyelitis Virus (MEF1) as Determined by Electron Microscopy**
C. E. SCHWERDT, R. C. WILLIAMS, W. M. STANLEY, F. L. SCHAFFER, and M. E. MCCLAIN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 310–312, June, 1954. 2 figs., 14 refs.

For purposes of electron microscopy the authors, working at the University of California, purified and concentrated a litre pool of the MEF1 strain of Type-2 poliomyelitis virus, grown in cultures of monkey kidney tissue, as follows: (1) isoelectric precipitation at *p*H 4; (2) resuspension of the precipitated virus in a one-tenth or one-twentieth volume of 0·94 M NaCl solution buffered at *p*H 7·8 with 0·02 M Na_2HPO_4 solution; (3) two *n*-butanol extractions of the saline extract of the precipitated virus; (4) concentration of the virus from the extracted aqueous phase by one cycle of differential ultracentrifugation with isotonic saline buffered at *p*H 7·8 as solvent; (5) treatment of the virus concentrate with crystalline ribonuclease and deoxyribonuclease; and (6) a final concentration and purification of the virus by a second cycle of differential ultracentrifugation.

Before preparing films for air-drying the virus suspension was dialysed against 0·1 M ammonium acetate. For freeze-drying they were dialysed against 0·1 M sodium bicarbonate. The films were irradiated with ultraviolet light sufficiently long to render the virus non-infective, shadowed with uranium, and photographed with the electron microscope. Two electron micrographs at a magnification of ×74,000 are reproduced, showing spherical particles of uniform diameter. The freeze-dried particles are stated to be truly spherical in shape, with a diameter of 27 mμ, whereas those which had been air-dried are slightly flattened, with a diameter of 31 mμ. *R. Hare*

39. **Comparison of Methods for Recovering Poliomyelitis Viruses from Human Sources**
H. A. WENNER and C. A. MILLER. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 11–15, May, 1954. 14 refs.

A total of 104 fecal and oropharyngeal specimens obtained directly from human sources were studied in three types of tissue culture. The virus recovery rates among fecal samples were of the same order, regardless of the type of tissue culture used. Under the conditions of the study, monkey kidney epithelial cell cultures were superior to HeLa or testicular cultures in the primary isolation of poliomyelitis virus from oropharyngeal specimens. A comparison of tests with fecal samples in monkeys and in tissue culture indicated that the latter was as good as, if not better than, monkeys in detecting poliomyelitis virus.—[From the authors' summary.]

40. **Quantitative Studies on Excretion of Poliomyelitis Virus: a Comparison of Virus Concentration in the Stools of Paralytic and Non-paralytic Patients**
R. WARD, G. A. LOGRIPPO, I. GRAEF, and D. P. EARLE. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 354–357, March, 1954. 14 refs.

In a study of the titre of virus in the stools of poliomyelitic patients, carried out at New York University College of Medicine, the stools of 21 patients suffering from poliomyelitis during the epidemic of 1949 in New York City were collected during the first week of the illness and again 7 days later. They were extracted with water, treated with ether, and centrifuged. The supernatant was titrated for virus content by injection into immature rhesus monkeys, and by inoculation of monkey testicular-tissue cultures.

It was found that the virus titres of extracts of faeces obtained from patients with the paralytic form of poliomyelitis were significantly higher than those from non-paralytic cases. There was fairly good agreement between the titres as determined in monkeys and in tissue cultures in respect of faeces obtained in the first week of the disease, but the second-week extracts were markedly more virulent for tissue cultures than for the monkeys, the titres being nearly 100 times higher. The authors suggest that a likely source of variants of the poliomyelitis virus possessing lowered pathogenicity for primates would be the stools of poliomyelitic patients after the first week of illness. *M. H. Salaman*

41. **Propagation in Tissue Cultures of Cytopathogenic Agents from Patients with Measles**
J. F. ENDERS and T. C. PEEBLES. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 277–286, June, 1954. 7 figs., 17 refs.

Throat washings, venous blood, and faeces obtained from 7 patients at the Children's Medical Center (Harvard Medical School), Boston, in the early stages of measles were inoculated into roller-tube cultures of a variety of different tissues in a medium containing 90% bovine amniotic fluid, 5% beef embryo extract, and 5% horse serum, together with antibiotics and phenol red. The medium was changed at intervals of 4 to 5 days. An agent was isolated by this method which passed through a sintered glass filter and was destroyed by heating at 65° C. for 30 minutes. It could be serially transferred by inoculating the fluid of cultures at any time from the 4th to 16th day into fresh cultures. As many as 10 passages were carried out with one strain. The agent was isolated from the blood or throat of 5 patients, but could not be detected in the faeces of 3

of them. A variety of cells were employed, the best growth and most marked changes being seen in cultures of renal epithelium from man or the monkey.

The agents isolated in this way induced changes which suggested the coalescence of many cells to form large, vacuolated giant cells containing many nuclei. Changes were also observed in the nuclei, the centre being occupied by an apparently homogenous acidophilic substance, the chromatin being displaced to the margin in the form of a deeply staining dense ring or crescent. The cytopathogenic effect was neutralized by the serum of convalescents, and complement fixation was demonstrated when the crude, undiluted culture fluid was added to convalescent serum. The antibody detected in this way appeared as early as the 7th day and was still present 2 months later.

R. Hare

42. **The Release of Influenza Virus from the Infected Cell**

L. HOYLE. *Journal of Hygiene* [*J. Hyg. (Lond.)*] **52**, 180–188, June, 1954. 22 figs., 16 refs.

Examination by dark-ground microscopy of detached portions of the chorio-allantoic membrane of normal fertile eggs showed that spherical and tubular protrusions develop from the cell margins and soon become detached. When the cells are infected with influenza-A virus this phenomenon is more obvious, and tubular protrusions are much commoner. These tubular protrusions may fragment into spherical particles which undergo contraction in size, probably by loss of water, and it is these particles, consisting of a closely aggregated mass of virus protein surrounded by a membrane derived from the host cell, which the author considers to be the fully-formed infective particle of this virus. The filaments frequently seen in the allantoic fluid of eggs infected by this virus would appear to be contracted tubular protrusions which have not undergone fragmentation into elementary particles.

R. Hare

SEROLOGY AND IMMUNOLOGY

43. **Inhibition of Growth of Pleuro-pneumonia-like Organisms by Antibody**

D. G. ff. EDWARD and W. A. FITZGERALD. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 23–30, 1954. 4 figs., 6 refs.

Working at the Wellcome Research Laboratories, Beckenham, Kent, the authors have carried out investigations on the power of antisera prepared against pleuropneumonia-like organisms (PPLO) to inhibit the growth of these organisms when incorporated in culture media. Antisera against living PPLO were prepared in rabbits and used both for agglutination tests against live organisms and for incorporation in horse-serum–agar plates in a series of dilutions ranging from 1 in 25 to 1 in 1,000. Plates containing normal rabbit serum at a dilution of 1 in 25 were similarly treated as a control.

It was found that whereas normal growth occurred on the control plates, growth was inhibited on the plates containing antiserum of the homologous organism and of those serologically related to it; the growth of serologically unrelated organisms was not affected. The ability to inhibit growth in this way bore no relation to the agglutinating titre of the serum, and appeared to be due to a different antibody from that involved in agglutination. The ability was also independent of the presence of complement. The rate of killing of the organisms by the antibody and the morphological changes produced in them during the process are described.

A number of ordinary bacteria were also tested in a like way for inhibition of growth by specific antiserum, but with negative results. A serum prepared against the L phase of *Proteus vulgaris*, however, inhibited its growth but not that of the parent organism (the bacillary phase). The authors suggest that the method described might be used in preference to the agglutination reaction in the examination of large numbers of strains isolated from the human genital tract.

John M. Talbot

44. **Studies on Local Antibody Production. Demonstration of Agglutination by Lymphocytes**

S. P. HAYES and T. F. DOUGHERTY. *Journal of Immunology* [*J. Immunol.*] **73**, 95–99, Aug., 1954. 7 figs., 27 refs.

45. **The Antigenic Structure of *Mycobacterium tuberculosis*, var. *hominis***

G. G. MEYNELL. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **67**, 137–150, 1954. 40 refs.

It was first shown by Keogh *et al.* (*Nature*, 1947, **160**, 63) that the polysaccharide component of bacteria is usually adsorbed on to normal erythrocytes, but that the protein fraction is not. Later Boyden (*J. exp. Med.*, 1951, **93**, 107) succeeded in showing that protein antigens were adsorbed on to erythrocytes which had been previously treated with tannic acid. The present author, working at the London School of Hygiene and Tropical Medicine, has found that the polysaccharide and protein antigens present in the purified protein derivative of tuberculin (P.P.D.) can be separated by employing selective methods based on the above [Chen and Meyer (*J. Immunol.*, 1954, **72**, 282) have recently studied the antigenic structure of *Pasteurella pestis* by similar means]. Other tuberculo-polysaccharide preparations were also examined, but normal erythrocytes were less easily sensitized by these extracts than by P.P.D.

Antibodies to the polysaccharide were readily produced by injecting into rabbits either living or killed tubercle bacilli. Antibodies to the protein fraction of P.P.D. were often found in the serum of infected guinea-pigs, but not in the serum of tuberculous patients. Rabbits given small doses of killed human-type organisms intravenously failed to produce antibody to the protein fraction, but the intramuscular injection of P.P.D. or of dense suspensions of killed tubercle bacilli in liquid paraffin yielded satisfactory antisera. Absorption of the antisera containing the various high-titre antibodies with bacillary suspensions of increasing density removed the anti-polysaccharide and anti-phosphatide antibodies, but the titre of the anti-protein antibody was hardly affected. It is suggested that in the

intact tubercle bacillus the polysaccharide and phosphatide fractions are present as surface antigens, while the protein fraction, which is also found in P.P.D., is a deep antigen.

Full details are given of preparation of the various reagents used and also of the techniques employed.

H. J. Bensted

46. **Some Observations on the Nature of the Antigens in the Cell Wall of *Corynebacterium diphtheriae***

C. S. CUMMINS. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **35**, 166–180, April, 1954. 4 figs., 25 refs.

The antigenic constituents of the cell wall of a *mitis* strain of *Corynebacterium diphtheriae* were investigated at the London Hospital Medical College in experiments with suspensions of intact bacteria and of cell-wall material obtained by mechanical disintegration of the organisms, followed in some cases by digestion with trypsin, papain, or pepsin. Two separate antigens were demonstrated—a superficial specific antigen and a deeper group antigen.

Intact bacteria treated with enzymes were unstable in suspension and were therefore unsuitable for agglutination experiments, but absorption experiments with such bacteria in suspension showed that the antigen responsible for type-specific agglutination was destroyed almost completely by pepsin acting for 24 hours, whereas with papain and trypsin the loss of antigen was considerably smaller. The specific antigen was present in crude cell-wall preparations, as these absorbed specific antibodies from sera prepared against whole organisms. On the other hand crude cell-wall material was agglutinated by homologous and heterologous sera prepared against intact cells. It was also possible to remove antibodies to cell-wall suspensions by absorption with cell-wall material from a different strain, leaving the titre of specific antibodies unaltered. The titres of homologous and heterologous sera for cell-wall suspensions were almost identical.

Electron micrographs of the crude cell-wall material showed that a great deal of dense material still adhered to the wall. Digestion with a 1-in-20 dilution of liquor trypsin co. for 3 to 4 hours removed almost all the denser material with preservation of the specific antigen, while pepsin treatment for 20 hours at 37° C. and *p*H 2 almost entirely destroyed the specific antigen, as with intact bacteria. Crude cell-wall preparations treated with trypsin and papain continued to give cross-agglutination with heterologous sera that did not agglutinate intact bacteria. Cell-wall preparations from a *gravis* or an *intermedius* strain were capable of removing completely all antibodies to the cell wall of the *mitis* strain, while leaving the titre of specific antibodies unchanged.

The specific antigen disappeared from suspensions of intact cells almost completely after heating for 3 hours at 100° C., while the group-antigen content of a corresponding purified cell-wall preparation was not affected even after 6 hours at 100° C. Periodate oxidation of a purified cell-wall preparation resulted in complete disappearance of the group antigen. It seemed probable, therefore, that the group antigen is of a polysaccharide nature, since it remains unaltered by the action of proteolytic enzymes and heat but is destroyed very rapidly by periodate oxidation, while the specific antigen, as present in control suspensions of intact bacteria, is destroyed only after 18 to 24 hours' exposure to periodate.

Purified cell-wall preparations of *C. xerosis*, *C. hofmanni*, and *C. renale* were not agglutinated to any significant degree by a serum against a purified cell-wall preparation of *mitis*-type *C. diphtheriae*. However, a purified cell-wall preparation of *C. ovis* was agglutinated to half-titre by such a serum. This finding could be confirmed by absorption tests with the same preparations and serum.

The author suggests that the demonstration and identification of the superficial, heat-labile, specific antigens, which are of a protein nature, and the deeper, heat-stable, group antigen, probably of a polysaccharide nature, may prove useful in the classification of these organisms.

K. Zinnemann

47. **Protective Antigen of *Haemophilus pertussis***

L. PILLEMER, L. BLUM, and I. H. LEPOW. *Lancet* [*Lancet*] **1**, 1257–1260, June 19, 1954. 5 figs., 8 refs.

In a preliminary report (*Proc. Soc. exp. Biol.* (*N.Y.*), 1950, **75**, 704) the senior author has shown that a protective antigen could be extracted from *Haemophilus pertussis* by sonic disintegration and made to combine irreversibly with human erythrocyte stromata, and that this stromata–protective-antigen complex (S.P.A.) was highly protective to mice against cerebral infection with *H. pertussis*.

In the present article from Western Reserve University, Cleveland, Ohio, the authors describe: (1) the method of growing *H. pertussis* (Strain 134) for preparation of a suspension; (2) the type of sonic oscillator used; (3) the method of liberating the protective antigen by sonic disintegration; (4) the method of preparing a sterile suspension of stromata from Group-O, Rh-negative blood; (5) the optimum conditions for the interaction of the antigen with the stromata; and (6) the preparation of S.P.A. on a large scale. Full technical details of every step are given [but for these the original article should be consulted].

In tests on mice receiving intracerebral injections of *H. pertussis* the protective effect of S.P.A. was compared with that of the U.S. National Institutes of Health pertussis reference vaccine; S.P.A. was shown to be 4 to 6 times as potent as the reference vaccine. The antigen is apparently not associated with pertussis haemagglutinin, nor is it associated with pertussis toxin since it did not kill mice by intravenous injection or cause necrosis of the rabbit's skin, nor with pertussis agglutinogen as it produces little or no agglutinins in mice. In fact the protective antigen bears no resemblance to any of the pertussis antigens so far isolated. Preparations of S.P.A. are stated to keep for many months. Its efficacy as a prophylactic against whooping-cough can be tested only by extensive controlled trials, which are already in progress.

L. J. M. Laurent

Pharmacology

48. **Pamine Bromide: Gastric Antisecretory Effects and Therapeutic Usefulness in Peptic Ulcer and Other Gastrointestinal Disorders**
J. B. KIRSNER, E. LEVIN, and W. L. PALMER. *Gastroenterology* [*Gastroenterology*] **26**, 852–867, June, 1954. 6 figs., 6 refs.

"Pamine" bromide is the *n*-methyl bromide of the tropic acid ester of epoxytropine. It has been shown previously to have antisecretory and ulcer-preventing activity in rats and dogs and to reduce the fasting gastric secretion in patients with duodenal ulcer. In this report from the University of Chicago and Cleveland City Hospital it is stated that 0·014 to 1·4 mg. of pamine given intramuscularly abolished the basal secretion of gastric acid in 25 of 47 patients with duodenal ulcer, the effect lasting in 10 tests for over 3 hours. It was also effective when given by intragastric or intraduodenal instillation, anacidity occurring in 24 of 63 patients receiving doses of 5 to 25 mg., while a single dose of 2·5 mg. reduced, but did not abolish, acid secretion. Side-effects, pronounced with doses of 15 mg. or more, occurred in 32 of these 63 patients. Comparable tests with hyoscine showed that it was less effective than pamine, and it seems unlikely that the action of pamine depends on its conversion in the body to hyoscine. Pamine was not very effective in reducing the high rate of secretion due to repeated injections of a histamine-like substance, doses of 0·13 to 0·23 mg. given intramuscularly reducing the rate of secretion briefly in 5 of 8 patients, but acid secretion being abolished for 30 minutes in only one.

During the prolonged treatment of 15 patients with pamine, usually for 14 to 23 weeks, there was a sustained reduction of fasting gastric secretion and occasionally complete anacidity; in 13 of the 15 patients the output of acid on repeated testing was consistently reduced by at least 50%. In a further trial the drug was given by mouth to 88 patients with peptic ulcer. A favourable clinical response was obtained in 62 patients, of whom 42 reported side-effects, constipation being the most troublesome. Usually 5 mg. 2 to 4 times a day was adequate. In 17 cases the drug was stopped because of side-effects and in 9 cases for other reasons. Such side-effects often decreased or subsided as treatment was continued. No demonstrable toxic effects were noted after prolonged treatment.

Probably because it decreases gastrointestinal motility pamine had a favourable or good effect in 24 of 37 patients with other gastrointestinal diseases. Diarrhoea was relieved in 22 of these. Once again side-effects were reported by a relatively high proportion of patients (25 of 37), and in 11 cases the drug had to be stopped for this reason.

It is considered that this substance represents an advance towards the objective of "the ideal gastric antisecretory agent, completely suppressing the output of hydrochloric acid for long periods after oral administration and highly effective in the treatment of peptic ulcer, without unpleasant side-effects". *Derek R. Wood*

49. **Effects of Histamine and Epinephrine on the Small Pulmonary Blood Vessels of Living Rabbits**
W. S. BURRAGE, J. W. IRWIN, J. I. GALLEMORE, and D. M. K. WANG. *Journal of Allergy* [*J. Allergy*] **25**, 293–301, July, 1954. 9 figs., 16 refs.

In experiments on more than 200 anaesthetized rabbits, carried out at the Massachusetts General Hospital (Harvard Medical School), Boston, the thoracic wall over a small area of lung surface was removed and the blood vessels in this area kept under microscopical observation. The intravenous injection of 5 mg. of histamine caused marked dilatation of the capillaries, the blood flow being rapid at first, but slowing down and stagnating later. Arterioles and venules showed a transient decrease in diameter. In those animals which survived, the dilatation of the capillaries persisted for a long time, but the blood flow in them increased to its previous speed. In such animals a further injection even of a large dose (50 mg.) of histamine had no effect at all. In those animals which subsequently died in histamine shock the capillaries showed marked dilatation and the linear blood flow stopped immediately, although the heart was still beating. Adrenaline in doses of 0·2 to 0·9 ml. of 1-in-100,000 solution per kg. body weight given intravenously caused a constriction of the pulmonary arterioles, with reduced and sometimes oscillating blood flow. After one minute the constriction changed to dilatation and the blood flow became very rapid. *H. Herxheimer*

50. **The Cardiovascular and Renal Hemodynamic Response to the Administration of Reserpine (Serpasil)**
J. H. MOYER, W. HUGHES, and R. HUGGINS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 640–648, June, 1954. 2 figs., 4 refs.

At the Jefferson Davis Hospital (Baylor University), Houston, Texas, the authors have studied the effects of reserpine, a pure alkaloid from *Rauwolfia serpentina*, on dogs and human beings. Anaesthetized dogs were given 3 or 4 mg. intravenously, and 1 to 2 hours later the blood pressure was usually moderately decreased and remained so for 2 to 5 hours; there was no consistent effect on cardiac output. The acute renal haemodynamic response to intravenous reserpine was observed in 10 dogs and in 6 patients with hypertension. The dogs were given 2 to 4 mg. of reserpine intravenously and again a delayed hypotensive effect was noted, unassociated with significant alterations in glomerular filtration rate or in renal plasma flow; there was no consistent effect on sodium and potassium excretion or on their concentration in the plasma. When a 1-in-100,000 solution of noradrenaline was infused intravenously 4 hours after the administra-

tion of reserpine the usual renal haemodynamic response was not altered by the presence of reserpine: as the blood pressure increased, the renal blood flow decreased.

Of 6 hypertensive patients who each received 1 to 3 mg. of reserpine as an intravenous infusion in 100 ml. of 5% glucose solution over a period of 10 to 20 minutes, 5 showed some slight reduction in blood pressure; the 6th developed severe hypotension requiring the administration of noradrenaline. Hypotension began at least one hour after injection of reserpine and reached a maximum at 3 hours. There were no consistent effects on glomerular filtration rate, renal blood flow, sodium or potassium excretion, or the plasma levels of these ions. The effects of prolonged oral administration were observed in 8 additional patients with hypertension, each of whom received 3 to 6 mg. of reserpine daily for 3 months; 6 of them showed a significant reduction in mean blood pressure. There was no evidence of depression of renal function or of excretion of electrolytes, and plasma sodium and potassium levels were unchanged.

The study confirms that reserpine is only moderately potent in reducing blood pressure, and suggests that it has no significant action on the kidney.

Thomas B. Begg

51. **Ventricular Function. V. The Circulatory Effects of "Aramine"; Mechanism of Action of "Vasopressor" Drugs in Cardiogenic Shock**

S. J. SARNOFF, R. B. CASE, E. BERGLUND, and L. C. SARNOFF. *Circulation* [*Circulation (N.Y.)*] **10**, 84–93, July, 1954. 7 figs., 12 refs.

In the normal anesthetized dog "aramine" produces a slight to moderate elevation of arterial pressure and a bradycardia. When the bradycardia is abolished either after vagotomy or during hemorrhagic hypotension aramine produces marked elevations of arterial pressure.

The effects of the drug on cardiac output, coronary flow, atrial and arterial pressures and peripheral vascular resistance have been presented. In small doses it produces a striking improvement in the ventricular function curves of both the right and left ventricles (more stroke work at any given filling pressure). Subsequent doses do not further improve myocardial contractility but do increase peripheral vascular resistance and tone. This bivalent effect on heart and periphery was also demonstrated by a time-dissociation technic.

The myocardium does not require a greater coronary flow per unit of work after the administration of aramine. Acute coronary insufficiency was induced by adjusting a clamp on the tube feeding the left main coronary artery. This produced a fall in arterial pressure, cardiac output, and ventricular stroke work, and a rise in left atrial pressure. The subsequent intravenous injection of aramine (with the screw clamp still in place) returned these values to or near their control levels.

The authors seriously question the premise that an agent for treating the hypotension of cardiogenic shock should achieve its effect solely or predominantly by producing peripheral vasoconstriction.—[Authors' summary.]

M.—C

52. **The Action of *Ornithogalum umbellatum* on the Heart**

R. A. WAUD. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **111**, 147–151, June, 1954. 2 figs., 6 refs.

It has been shown that *Ornithogalum umbellatum* (Star of Bethlehem), a bulbous plant belonging to the lily family, contains a substance having an action very similar to, if not identical with, that of the glycosides of digitalis.

Active extracts were prepared with alcohol, acetone and with water and standardized on frogs and cats. The most active bulbs, when assayed by the cat method, showed a potency 1·84 times that of digitalis leaves. —[Author's summary.]

53. **The Action of Procaine and Procaine Amide on the Heart**

P. SZEKELY and N. A. WYNNE. *British Heart Journal* [*Brit. Heart J.*] **16**, 267–272, July, 1954. 4 figs., 23 refs.

54. **Disposition of Intra-articularly Injected Hydrocortisone Acetate, Hydrocortisone and Cortisone Acetate in Arthritis. I. Concentrations in Synovial Fluid and Cells**

M. ZACCO, E. M. RICHARDSON, J. O. CRITTENDEN, J. L. HOLLANDER, and F. C. DOHAN. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **14**, 711–718, July, 1954. 3 figs., 6 refs.

Studies have been made in an effort to gain some understanding of the reason for the difference in anti-arthritic effect of intra-articular injections of cortisone and hydrocortisone. The results are as follows: (1) The rates of decrease in concentration of 17-hydroxycorticoids in the joint fluid during the first few hours after intra-articular injections of hydrocortisone, hydrocortisone acetate and cortisone acetate are approximately the same, the effect of differences between some clinical subjects being greater than that of differences between compounds. (2) The hydrolyzed forms of both hydrocortisone acetate and cortisone acetate were present in greater proportions in the fluid than in the cells. (3) The proportion of 17-hydroxycorticoids present in the cells after injection of cortisone acetate is greater than after the injection of the free form of hydrocortisone, but less than after the injection of hydrocortisone acetate. These data do not afford an explanation for the difference in anti-arthritic effect between hydrocortisone and cortisone. Further studies are in progress.—[Authors' summary.]

55. **Morphine Derivatives with Antianalgesic Action**

A. F. GREEN, G. K. RUFFELL, and E. WALTON. *Journal of Pharmacy and Pharmacology* [*J. Pharm. Pharmacol.*] **6**, 390–397, June, 1954. 14 refs.

A series of *n*-alkyl substituted derivatives of morphine has been synthesised and examined for analgesic and antianalgesic action. Several of these compounds have shown powerful antianalgesic activity, *n*-propylnormorphine and the diacetyl and dipropionyl derivatives of *n*-allylnormorphine (nalorphine) being about as active as nalorphine.—[Authors' summary.]

Chemotherapy

56. **The Binding of Penicillin in Relation to its Cytotoxic Action. II. The Reactivity with Penicillin of Resistant Variants of Streptococci, Pneumococci, and Staphylococci**
H. EAGLE. *Journal of Experimental Medicine* [*J. exp. Med.*] **100**, 103–115, July, 1954. 2 figs., 9 refs.

Continuing an investigation of the penicillin-binding activity of bacteria (*J. exp. Med.*, 1954, **99**, 207; *Abstracts of World Medicine*, 1954, **16**, 188) the author, in the present paper, attempts to clarify the relationship between penicillin and bacteria which have been rendered resistant to this antibiotic. At the U.S. National Microbiological Institute, Bethesda, Maryland, 4 bacterial species—*Streptococcus haemolyticus*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Streptococcus faecalis*—were made penicillin-resistant by selective propagation through increasing concentrations of the antibiotic. The reactivity of these species and of their cell-free sonic extracts was determined by using penicillin labelled with radioactive sulphur to measure the degree of combination. The results were variable; some resistant strains bound more penicillin, some were unchanged in their reactivity, and some bound less penicillin, in comparison with the sensitive parent strain. The development of resistance was not necessarily related to decreased reactivity with the antibiotic, nor was it accompanied by an increased capacity to degrade penicillin, either extracellularly or within the cell. It is suggested that resistance to the cytotoxic action of penicillin may be due to decreased reactivity of some vulnerable cell component as yet unrecognized. *D. Geraint James*

57. **The Binding of Penicillin in Relation to its Cytotoxic Action. III. The Binding of Penicillin by Mammalian Cells in Tissue Culture (HeLa and L Strains)**
H. EAGLE. *Journal of Experimental Medicine* [*J. exp. Med.*] **100**, 117–124, July, 1954. 2 figs., 8 refs.

One of the most striking features of penicillin is its lack of toxicity for mammalian cells in tissue culture. In this further paper on the binding of penicillin [see Abstract 56] the author describes experiments undertaken to determine the fate of penicillin in tissue-culture cells. Two cell lines were used—the L strain of mouse fibroblasts and the HeLa strain cultured from a human uterine carcinoma. The degree of binding was determined by using penicillin labelled with radioactive sulphur. The cultured cells failed to bind and concentrate penicillin in the same way as sensitive bacteria. The large cellular content of penicillin immediately after exposure and the ease with which biologically active antibiotic could be removed by washing excluded the possibility of impermeability of the cell to penicillin or intracellular degradation of the antibiotic. It seemed more likely that lack of binding was due to weak reactivity of mammalian cells to the drug, the cells behaving like penicillin-resistant bacteria. It is suggested that the relative non-toxicity of penicillin to mammalian cells or to such cells in culture is related to this low reactivity with the antibiotic. *D. Geraint James*

58. **Clinical Findings in Patients Treated with a New Combination of Antibiotics: Procaine Penicillin, Dibenzylethylenediamine Penicillin, and Dihydrostreptomycin**
I. SCHIFF. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 944–947, Sept., 1954. 18 refs.

59. **Erythromycin Suspension in Children**
G. B. GATTMAN and I. ROSENBAUM. *Journal of Pediatrics* [*J. Pediat.*] **44**, 547–552, May, 1954. 5 refs.

In this paper from Indianapolis General Hospital the authors report their experience with a suspension of erythromycin (" ilotycin ") in the treatment of a variety of infections, mostly respiratory, in 31 children. The drug was given in a dosage of 5 mg. per lb. (11 mg. per kg.) body weight 6 hourly for 5 to 11 days. All the patients recovered, and the only toxic effect possibly due to the drug was vomiting in one case. Cephalin flocculation tests were performed in all cases on admission and again before leaving hospital in order to detect any liver damage which might have been caused by the drug; no evidence of such damage was noted.

The authors conclude that the preparation of cinnamon-flavoured suspension of erythromycin ethyl carbonate used by them has promise in the treatment of common respiratory-tract infections in young children. *T. Anderson*

60. **Quantitative Observations on the Pattern of Emergence of Resistance to Isoniazid**
R. TOMPSETT. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 91–101, July, 1954. 11 figs., 14 refs.

At the New York Hospital–Cornell Medical Center, New York, the author investigated *in vitro* the susceptibility to isoniazid of tubercle bacilli isolated from the sputum or gastric aspirate of 47 patients. Quantitative determination of the proportions of bacilli susceptible and resistant to isoniazid showed, even in this small group of patients, wide variations in the speed and magnitude of the development of resistance. The degree of resistance developed was particularly marked with the lowest concentration of isoniazid employed (0·1 μg. per ml.). In 9 out of 11 instances, however, a preponderance of cells in the culture continued to be inhibited by 1·0 μg. of isoniazid per ml., a concentration which is readily attained *in vivo*.

The author considers that the heterogeneity of the bacterial populations in the cultures examined indicates that " great caution should be exercised in interpretation of any culture as ' resistant ' ". *A. W. H. Foxell*

Infectious Diseases

61. **Sarcoidosis with Involvement of the Nervous System. Report of Nine Cases**
O. HÖÖK. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **71**, 554–575, May, 1954. 6 figs., bibliography.

The author presents, from the Serafimer Hospital, Stockholm, 9 cases of Boeck's sarcoidosis in which there was involvement of the nervous system. There appear to be no signs or symptoms which are pathognomonic of sarcoidosis, and in the present series the neurological picture varied considerably. There were ocular lesions in 3 cases and mild or severe mental disorder in 5. In one of the latter the intracranial pressure was raised owing to an obstruction of the right lateral ventricle by a granulomatous mass probably originating in the choroid plexus. In another case there was evidence of a space-occupying lesion with focal signs, which regressed spontaneously in about 2 months; pneumoencephalography and carotid arteriography revealed poorly vascularized expanding processes in the anterior part of the left frontal region. These last 2 cases illustrate how sarcoidosis may produce symptoms resembling those of cerebral tumour.

Four patients suffered from facial palsies unrelated to parotid swellings; in one case the palsy was recurrent. Further neurological signs were: facial sensory loss in one case, transient nerve deafness in 2, unilateral pharyngeal paralysis in one, and recurrent papillitis and Argyll Robertson pupils in one case each. In 6 cases there was either a raised protein content or pleocytosis, or both, in the cerebrospinal fluid.

The average follow-up period was 5 years. In most of the patients the neurological disorders had subsided or improved markedly. The prognosis in sarcoidosis, generally fairly good, is thought to be comparatively poor in cases with involvement of the nervous system.

L. G. Kiloh

62. **Skin Sensitivity in Sarcoidosis**
C. HOYLE, J. DAWSON, and G. MATHER. *Lancet* [*Lancet*] **2**, 164–168, July 24, 1954. 1 fig., bibliography.

A controlled investigation of tuberculin sensitivity in sarcoidosis is reported. Since the *Brucella* species, *Coccidioides immitis*, and *Histoplasma capsulatum*, have each been suspected to be the causative organisms of sarcoidosis, these were first excluded by examining the skin reaction of a group of patients with sarcoidosis to intradermal injection of antigens prepared from these organisms. No sign of brucellosis was found in 28 patients, while in 35 the reaction to intradermal injection of coccidioidin and of histoplasmin was negative.

It was found that sensitivity to tuberculin was present in a higher proportion of patients with sarcoidosis than has hitherto been reported, showing that a positive reaction is no contraindication to a diagnosis of sarcoidosis. The comparatively low incidence of tuberculin sensitivity (28%) paralleled that observed in cases of Hodgkin's disease and other reticuloendothelioses. Liver biopsy is recommended as the best diagnostic procedure in sarcoidosis.

Geoffrey McComas

63. **Latent Congenital Toxoplasmosis.** (Latente konnatale Toxoplasmose)
J. PAUL. *Klinische Wochenschrift* [*Klin. Wschr.*] **32**, 485–491, June 1, 1954. 1 fig., 15 refs.

By performing the dye test of Sabin and Feldman on sera from 428 infants not suspected of having toxoplasmosis the author, working at the Paediatric Clinic of the University of Erlangen, was able to confirm that in a proportion of cases antibodies against the disease derived from the mother persist in the infant circulation for as long as 5 months. In 5 cases titres of 1 in 64 or higher were found during the first 3 years of life. One of these babies had gastro-enteritis, one vaccinal encephalitis, one pertussis encephalitis, and 2 had tuberculous meningitis. Relying mainly on the abnormally high dye-test findings for babies of this age, the author concludes that these were primarily cases of latent intrauterine *Toxoplasma* infection in which the triad of hydrocephalus, intracerebral calcification, and choroidoretinitis had not yet developed, the assumption being made that the damage to the brain caused by the infection predisposes to attack by other agents likely to damage the central nervous system. [Confirmation of the dye-test results by complement-fixation tests is not reported.]

I. A. B. Cathie

64. **The Antitoxoplasmic Activity of "Puromycin"**
D. E. EYLES and N. COLEMAN. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 649–652, June, 1954. 3 refs.

"Puromycin" [obtained from *Streptomyces albonicer*] prolonged the life of mice infected with *Toxoplasma gondii*, but treatment for as long as 28 days did not result in survival of mice. All mice eventually relapsed and died of toxoplasmosis or showed *Toxoplasma* organisms post mortem. On the basis of the activity of puromycin in mice it would appear that the drug is not sufficiently effective to be of practical value as an antitoxoplasmic agent.—[From the authors' summary.]

65. **The Treatment of Amebiasis with Arsthinol (*N.N.R.*) (Balarsen)**
E. H. LOUGHLIN, A. A. JOSEPH, and W. G. MULLIN. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 647–648, June, 1954. 3 refs.

While treating early cases of yaws in Haiti with "arsthinol" (a stable combination of acetarsol with BAL) in single daily doses of 20 mg. per kg. body weight for

5 days, the authors observed that 24 of the patients, who were also infected with *Entamoeba histolytica*, had all lost this parasite after treatment with the drug. A second group of 16 patients with amoebiasis were treated with 15 mg. of arsthinol per kg. body weight daily for 10 days and in these, as well as in the original 24, the faeces were free of cysts for 6 weeks after treatment—this period being chosen since reinfection could reasonably be excluded only up to that point. In none of the 76 patients receiving arsthinol for one or both diseases were their any side-effects. In an addendum the authors refer to similar good results reported by Levy and Falley (*Gastroenterology*, 1952, **22**, 4). *I. M. Rollo*

66. **Iceland Disease A New Infection Simulating Acute Anterior Poliomyelitis**
D. N. WHITE and R. B. BURTCH. *Neurology* [*Neurology*] **4**, 506–516, July, 1954. 1 fig., 1 ref.

This paper describes an epidemic of what appeared to be an infectious disease which occurred in New York State in the late summer of 1950. The clinical features resembled those of poliomyelitis, but the disease appeared to constitute a distinct entity. The illness ran a febrile course, often with early symptoms suggestive of a respiratory or gastrointestinal infection. The most consistent feature, however, was soreness and tenderness of the muscles, particularly those of the neck and shoulders, accompanied by transient weakness without wasting. Sensory manifestations were not uncommon, and included paraesthesiae, cutaneous sensory loss, and loss of position sense. Emotional upsets were also noted. The muscle pains, sensory loss, and emotional disturbances persisted up to the time of follow-up examination 15 months later. No virus was isolated from these cases and serological examination provided no evidence of infection with poliomyelitis or other known viruses.

The authors conclude that although the symptomatology of this disease was in many respects similar to that of Coxsackie virus infection, the sensory involvement, together with the laboratory findings, rule out this diagnosis. They consider it likely that the infective agent was a neurotropic virus also affecting the muscles themselves, and draw attention to the similarity of the disease to that described by Sigurdsson *et al.* (*Amer. J. Hyg.*, 1950, **52**, 222; *Abstracts of World Medicine*, 1951, **9**, 209) which occurred in Iceland in 1948–9.

J. B. Stanton

67. **Family Infections by Coxsackie Viruses.** [In English]
T. JOHNSSON. *Archiv für die gesamte Virusforschung* [*Arch. ges. Virusforsch.*] **5**, 384–400, 1954. 1 fig., 10 refs.

At the Karolinska Institute, Stockholm, the author has conducted a systematic study of the familial occurrence of Coxsackie virus infections with a view to adding to the knowledge of their clinical manifestations and epidemiology. Eight family outbreaks involving 11 cases of infection were investigated, specimens for virological and serological examination being obtained not only from those affected, but also from other members of the family. In 3 families the viruses found belonged to Subgroup A and in 5 to Subgroup B. The symptoms for which these viruses were thought to be aetiologically responsible were grouped into 4 syndromes—aseptic meningitis, pleurodynia, myalgia, and minor illness. Most of the cases of meningitis were in children and were due to infection with Type-B3 virus. Pleurodynia and myalgia were more common in adults. Viruses of Subgroup A seemed to cause a smaller proportion of clinical infections and milder symptoms than those of Subgroup B. Neutralizing antibodies to the type of virus concerned occurred in high titre in the blood of the majority of members of each family, and in some cases a rise of titre during the acute phase of the infection was demonstrable. Subclinical infection occurred in a total of 11 symptomless persons, as shown either by the isolation of the virus or by demonstration of a rise in antibody titre.

It appeared from the fact that a single primary case usually occurred in each family that the infection was introduced by that member of the family and not through water or food. The fact that the secondary cases occurred more frequently among the siblings than the parents probably reflects the more intimate contact between the children of a family. *J. V. Armstrong*

68. **Studies on the Etiology of Bornholm Disease (Epidemic Pleurodynia). II. Epidemiological Observations.** [In English]
T. JOHNSSON. *Archiv für die gesamte Virusforschung* [*Arch. ges. Virusforsch.*] **5**, 401–412, 1954. 6 refs.

In this paper the investigation of an outbreak of Bornholm disease in 2 towns in Sweden in 1950 is described in which a total of 85 cases occurred, 25 of these being studied in hospital and a field survey of the epidemic region conducted. The study of the hospital cases included full serological and virological investigations.

In spite of the variation in clinical manifestations it was concluded that the epidemic was aetiologically homogeneous and caused by Coxsackie virus B3. This virus was recovered from the stools in 7 out of 20 cases in which they were examined for it, and antibodies to the virus were present in the blood in rising titre during the febrile stage and in high titre during convalescence in all 10 patients examined. The clinical manifestations ranged from aseptic meningitis (more common in children), pleurodynia (more common in adults), and myalgia to minor illnesses such as sore throat.

From the field study it was concluded that once the virus was introduced into a family it rapidly spread amongst the members, producing symptoms in the majority. No firm conclusions as to the mode of dissemination were drawn, but it is suggestive that the largest focus of infection was found in an area where sanitary conditions were unsatisfactory.

J. V. Armstrong

69. **The Prevention of Deformity in Poliomyelitis**
J. M. P. CLARK. *British Medical Journal* [*Brit. med. J.*] **2**, 669–672, Sept. 18, 1954. 3 figs., 4 refs.

Tuberculosis

DIAGNOSIS AND PROPHYLAXIS

70. **Results of the B.C.G. Campaign in Montreuil: 7,668 Vaccinations carried out between 1948 and 1953.** (Bilan de la campagne BCG dans la ville de Montreuil: 7,668 vaccinations de 1948 à 1953)
M. FOURESTIER, A. BLACQUE-BELAIR, G. BAISSETTE, M. LOUSTAU-CHARTEZ, E. DE SAINT-GERMAIN, and R. ROBERT. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd. (Paris)*] **138**, 275–284, June 1, 1954. 5 figs.

Between 1948 and 1953, 7,668 young people up to 19 years of age—over 10% of the total population—were vaccinated with B.C.G. in Montreuil, 5,956 of those vaccinated being between 5 and 14 years old. The annual morbidity figures from tuberculosis during this period in Montreuil are here compared with those from a comparable town in the same region where B.C.G. vaccination was not practised.

In 1948 in Montreuil the number of cases of primary tuberculosis in patients of 0 to 19 years notified per 100,000 population in that age group was 403, and in 1953 it was 107. The corresponding figures for the other town were 155 and 223. The decline in primary infections in Montreuil was particularly notable among children of school age, and in 1953 no case was notified in the age group 15 to 19 years, which by then consisted very largely of vaccinated subjects. Between 1948 and 1953 the number of notifications of secondary tuberculosis per 100,000 of the total population also fell in Montreuil, whereas it increased in the other town.

Although mortality from tuberculosis in Montreuil during this period fell slightly more steeply than in the other town and in France as a whole, the difference was not so striking as was the case with the morbidity figures. However, when the 80 suburban communes of the Seine Department are arranged in descending order of mortality from tuberculosis, the other town ranked 45th in 1945 and again in 1953, whereas Montreuil improved its position from 26th in 1945 to 51st in 1953.

T. M. Pollock

71. **Multiple Puncture and Intradermal BCG Vaccination. A Quantitative Comparison in Terms of Allergy Production**
A. GESER. *Diseases of the Chest* [*Dis. Chest*] **26**, 62–69, July, 1954. 2 figs., 6 refs.

The degree of tuberculin sensitivity produced by intradermal injection of B.C.G. vaccine was compared with that produced by the multiple-puncture method of giving the vaccine. The Mantoux test, with 0·0001 mg. of P.P.D., was carried out on 2,632 school children in a densely populated centre in Luzon in the Philippines, and to the 1,754 non-reactors B.C.G. vaccine was given, the two methods of administration being used alternately. The multiple-puncture method consisted in making 40 punctures with a straight surgical sewing needle through one drop of the vaccine smeared over an area of skin measuring 2 by 4 cm. When 16 weeks had elapsed from the time of vaccination the tuberculin test was repeated with the same strength of P.P.D. as that used initially. It was found that the average diameter of the tuberculin reaction in children vaccinated intradermally was 12 mm., whereas it had an average diameter of 7·4 mm. in those vaccinated by the multiple-puncture technique. *T. M. Pollock*

72. **Five Years' Experience of B.C.G. Vaccination in Dublin**
M. DUNLEVY. *Medical Officer* [*Med. Offr*] **92**, 53–56, July 30, 1954. 15 refs.

An account is given of the City of Dublin B.C.G. Vaccination Scheme from its inception in October, 1948, up to the end of 1953, during which time over 32,000 persons were vaccinated. This figure includes some 5,000 newborn infants, the routine vaccination of whom was started at the Rotunda and Coombe Maternity Hospitals in September, 1950. A dose of 0·1 ml. of the Danish vaccine was used for all age groups, divided between 3 intradermal injections at the insertion of the left deltoid muscle. Regional adenitis was noted in 52 (1·51%) of 3,439 newborn infants (excluding those vaccinated most recently), with abscess formation in 21 of these (0·61%)—slightly lower figures than those reported by Purser (*Brit. med. J.*, 1954, **1**, 368; *Abstracts of World Medicine*, 1954, **16**, 192) for a similar series in Belfast. In children of other age groups the corresponding percentages were 0·45 and 0·15. Post-vaccinal Mantoux testing of newborn infants was carried out as a routine at 8 weeks and, if negative, repeated 2 months later (though in many cases the interval was longer), the agent used being P.P.D. in a dose of 100 t.u. The conversion rate among newborn infants in this series was 99.3%, and among children of other age groups 99·6%, while the reversion rates on retesting after a year were 1·8% and 1·03% respectively. These are much lower reversion rates than those found in surveys where Swedish vaccine has been used. *T. M. Pollock*

73. **The Comparison of Some Tuberculins in BCG-vaccinated and Unvaccinated Persons**
J. D. ARONSON, H. C. TAYLOR, and M. T. MCGETTIGAN. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 71–90, July, 1954. 32 refs.

The tuberculin test is widely used for diagnostic and epidemiological purposes and to assess the efficacy of B.C.G. vaccination. The variety of techniques and preparations of tuberculin now in use have, however, given rise to confusion, and this paper records a series of comparative tests carried out at the University of Penn-

sylvania and the Pennsylvania Bureau of Tuberculosis Control on both unvaccinated subjects and persons vaccinated with B.C.G. in order to determine the relative sensitivity of various different tuberculins, and of the intracutaneous and patch tests. Both old tuberculin (O.T.) and purified tuberculin (P.P.D.) were used, comparisons being made between the two types and also between different preparations of each type by means of simultaneous tests with paired tuberculins. The initial dose of O.T. given intradermally was 0·01 mg., and of P.P.D. either 0·00001 or 0·00002 mg., each in a volume of 0·1 ml., the results being read 48 hours later. The criteria used in determining the result are described.

Among unvaccinated persons significant differences were found both in the number of reactions obtained and in their degree between different samples of O.T. even from the same manufacturer. One sample which had been stored at room temperature for 25 years was still highly potent, whereas freeze-drying was shown to result in loss of potency. The purified tuberculins used included two samples of P.P.D. prepared by precipitation with trichloracetic acid—one from the State Serum Institute, Copenhagen, and the other from the Ministry of Agriculture Veterinary Laboratory, Weybridge—and two samples prepared by precipitation with ammonium sulphate (P.P.D.-S.)—one from the U.S. Public Health Service and one from another source. Compared with the P.P.D.-S. from the U.S.P.H.S., the Danish preparation gave the same proportion of reactions, although fewer of them were well marked, whereas the sample of Weybridge P.P.D. was more potent in both respects. The two samples of P.P.D.-S. showed no significant difference in potency. P.P.D.-S. prepared in tablet form was found to be less potent than standard P.P.D.-S. The relative potency of O.T. and P.P.D.-S. varied, some samples of O.T. being more potent and others less potent than P.P.D.-S.

When the potency of the different preparations of O.T. was compared by simultaneous tests on subjects who had been vaccinated with B.C.G. 2 months to 4 years previously, the differences were even more marked than in unvaccinated subjects. In comparative tests between a single preparation of O.T. and various purified tuberculins a significantly higher proportion of those vaccinated 2 to 3 months previously reacted to 0·1 mg. of O.T. than to 0·0001 mg. of P.P.D.-S., although the proportions reacting to the Danish and Weybridge preparations and to O.T. were much the same. In subjects vaccinated 1 to 4 years previously, however, the differences were very striking, a far higher proportion reacting to O.T. than to any of the purified tuberculins.

Comparative tests were also carried out between O.T. and samples of P.P.D. prepared from *Mycobacterium avium* and *M. balnei*. Among vaccinated persons the proportions reacting to O.T. and to P.P.D. from *M. avium* were comparable, whereas the proportion reacting was smaller with P.P.D. from *M. balnei* than with O.T. both in vaccinated and unvaccinated subjects.

The patch test (with O.T.) was shown to be less sensitive than the intracutaneous test with either O.T. or P.P.D.-S. in both vaccinated and unvaccinated subjects. *T. M. Pollock*

RESPIRATORY TUBERCULOSIS

74. Coexisting Pulmonary Coccidioidomycosis and Tuberculosis. A Review of Twenty-four Cases

B. H. Cotton, J. R. F. Penido, J. W. Birsner, and C. E. Babcock. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 109–120, July, 1954. 3 figs., 6 refs.

The authors describe 24 cases in which pulmonary coccidioidomycosis and tuberculosis co-existed, the diagnosis being confirmed in each case by sputum cultures and complement-fixation tests. Such cases might arise in 6 ways: (1) coccidioidal cavity with secondary infection by tuberculosis; (2) tuberculous cavity with secondary infection by *Coccidioides immitis*; (3) coccidioidal cavitation or infection in an area of dormant tuberculosis; (4) tuberculous cavitation in an area of coccidioidal granuloma; (5) simultaneous infection; (6) infection of separate areas of pulmonary tissue at different dates.

Nine of the cases in this series were treated successfully by pulmonary resection, which is considered to be the treatment of choice, particularly where cavities exist. The co-existence of these diseases should be carefully considered in patients who live in, or have visited, areas in which coccidioidomycosis is endemic.

A. Gordon Beckett

75. Infectivity of Pulmonary Tuberculosis in Relation to Sputum Status

J. B. Shaw and N. Wynn-Williams. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **69**, 724–732, May, 1954. 9 refs.

An investigation was carried out at the Luton and Bedford Chest Clinics in order to compare the risk of infection from three types of patient with pulmonary tuberculosis: (1) those in whom the sputum was positive for tubercle bacilli on direct examination (453 cases); (2) those in whom it was positive only on culture (230 cases); and (3) those in whom it was negative by both methods (321 cases). The presence of infection was determined, by radiological examination and tuberculin testing, in all contacts of each patient. (Contacts under 15 years of age were classed as children and those over that age as adults; only the children were tuberculin tested.) A group of 709 children who had no known contact with tuberculosis were tested as a control. A positive tuberculin-test reaction was included in the results if it occurred within 3 months of the discovery of the source case. For children up to 10 years of age tuberculin jelly was used, but in doubtful cases, as well as in those over 10 years of age, old tuberculin was used in dilutions up to 1 in 100.

The results, which are tabulated, showed that 65% of contacts of patients in Group 1 (sputum positive on direct examination) gave a positive skin reaction, compared with 26% of contacts of patients in Group 2, and 17% of contacts of patients in Group 3; of the children with no known contact, the skin test was positive in 22%. Among the 669 adult contacts and 374 child contacts

of the 453 patients in Group 1, 75 cases of tuberculosis were discovered in adults and 54 in children; while among the 408 adult and 228 child contacts of the 230 patients in Group 2, only 3 cases of tuberculosis in adults and 6 in children were found. The 354 adult contacts of the 321 patients in Group 3 were not kept under radiological supervision after the initial *x*-ray examination, but 5 cases of tuberculosis were reported among them and 2 cases of tuberculosis among the 221 child contacts.

T. M. Pollock

76. **Cortisone in the Treatment of Pulmonary Tuberculosis**

J. B. COCHRAN. *Edinburgh Medical Journal* [*Edinb. med. J.*] **61**, 238–249, July, 1954. 17 refs.

An interim report is presented from Dumfries and Galloway Sanatorium on the results of administration of cortisone to 9 patients (6 males, average age 45, and 3 females, average age 33) with pulmonary tuberculosis who had previously received streptomycin with PAS and/or isoniazid, the choice as regards the last two drugs depending on individual drug resistance, if any. All the patients had a positive sputum and moderate or advanced disease, 4 having bilateral lesions with cavitation. Streptomycin with PAS and/or isoniazid was known to be relatively ineffective in at least 2 of the patients.

Cortisone was given cautiously, the first patient receiving 12·5 mg., the second and third 25 mg., and the others 50 to 100 mg. daily, for 2 months. The other chemotherapeutic drugs were given at the same time and were continued for at least another 2 months after administration of cortisone ceased.

In all the patients there was initial symptomatic improvement, which was maintained in most of them. One patient died (the influence of cortisone in this case was uncertain); in the others an increase in weight, diminished cough, and an improvement in general condition and well-being were observed. A fall in the erythrocyte sedimentation rate was noted in 7 patients, but in most of them the rate promptly returned to the original level when cortisone was withdrawn. In 4 patients the radiological improvement was greater than could be expected from standard chemotherapy. With the possible exception of the fatal case, no adverse results of any consequence attributable to cortisone were observed. The author considers that the results warrant an extended trial of this form of treatment. The cases are reported in detail.

[The author's conclusion seems justified.]

R. J. Matthews

77. **Clinical Observations on the Use of Isoniazid in Tuberculosis**

H. M. PAYNE, R. L. HACKNEY, E. A. CLARK, and P. C. JOHNSON. *Diseases of the Chest* [*Dis. Chest*] **25**, 611–621, June, 1954.

Recording observations made at the College of Medicine, Howard University, Washington, D.C., on the results of isoniazid treatment in pulmonary tuberculosis, the authors deal particularly with the clinical and toxic effects of increasing the daily dosage to 7 to 13 mg. per kg. body weight. Of 31 patients who were already receiving 3 to 6 mg. per kg., 2 who had been losing weight gained weight when the dosage was increased; one showed no change in weight on either dosage; 8 who had been gaining weight on the lower dosage lost weight when it was increased; 7 who had also been gaining weight originally showed no further gain; and 13 gained weight on both dosages. Unusual symptoms during isoniazid treatment were noted in 5 of 69 patients receiving 3 to 6 mg. per kg. daily and in 7 of 28 receiving 7 to 13 mg. per kg. Evidence of eighth-nerve toxicity was judged by the response to caloric stimulation tests. Of 26 patients receiving more than 6 mg. per kg. of isoniazid daily for 1½ months or longer, 11 showed a loss of response to caloric stimulation. The results also indicated that the drug may accentuate vestibular damage when streptomycin has been given. Isoniazid did not appear to affect metabolism of glucose, as judged by the blood sugar levels in diabetic and non-diabetic patients. When the drug was given intramuscularly in a dosage of 100 mg. daily for 10 days patients complained of burning at the site of injection, but there were no general toxic effects. Injection of a molecular combination of streptomycin (1 g.) and isoniazid caused no general toxicity and only minimal local reaction. Examination of the cerebrospinal fluid withdrawn 2 hours after injection indicated that free streptomycin base was present. In specimens of blood withdrawn hourly there was an increasing titre of streptomycin up to 3 hours, and a decline in the isoniazid level after the first hour, although a level of 4 μg. of isoniazid per ml. was observed after the third hour.

T. M. Pollock

78. **Treatment of Pulmonary Tuberculosis with Isoniazide and Iproniazide**

S. COHEN and E. ANG. *Diseases of the Chest* [*Dis. Chest*] **25**, 622–639, June, 1954. 10 refs.

Experience with isoniazid and iproniazid in the treatment of patients with pulmonary tuberculosis at the Pollak Hospital for Chest Diseases, Jersey City, is described. A total of 76 patients were grouped and treated as follows. Group 1 comprised 59 patients, 34 of whom had already been treated with PAS and streptomycin and 25 of whom had not received chemotherapy; all the patients were given isoniazid in a dosage of 1 mg. per kg. body weight daily for the first 30 days, 2 mg. per kg. daily for the next 30 days, and 4 mg. per kg. for a further 30 days. At the end of 90 days 39 of the patients were available for further study and were regrouped and treated as follows: Group 1 (*a*), 22 patients in whom there was radiological improvement, received the maximum daily dose of isoniazid (4 mg. per kg. body weight) for 90 days; Group 1 (*b*), 6 patients whose radiographs showed no improvement, received 1 g. of streptomycin every third day and isoniazid daily for 90 days; and Group 1 (*c*), 11 patients who showed no radiological improvement but who had previously been treated with streptomycin, received 1 to 4 mg. of iproniazid per kg. body weight for 90 days. Group 2 contained the remaining 17 of the 76 patients. None of these had been treated with isoniazid before,

but 11 had had streptomycin previously; all were given iproniazid in a daily dosage of 1 to 4 mg. per kg. body weight for 90 days.

Of the 25 febrile patients in Group 1, 18 became afebrile, while all 9 febrile patients in Group 2 became afebrile. Whereas 80% of patients given isoniazid gained weight, all given iproniazid did so. There was no significant difference in the radiological findings between Group 1 and Group 2. Toxic manifestations, consisting of vertigo, nausea, vomiting, headache, delayed micturition, and involuntary muscle twitchings, were much more pronounced with iproniazid therapy; 2 cases of psychosis were noted among the patients treated with this drug. Albumin and erythrocytes were found in the urine of patients given either drug.

It is concluded that the toxic effects produced by iproniazid do not justify its use in "the average case of pulmonary tuberculosis". *T. M. Pollock*

79. **Isoniazid Therapy of Tuberculous Patients as a Preparation for Pulmonary Resection**
H. A. DICKIE, F. C. LARSON, and D. E. OLSON. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 102–108, July, 1954.

80. **The Continuous and Concurrent Use of Streptomycin, *para*-Aminosalicylic Acid, Isoniazid plus Early Surgery in the Treatment of Tuberculosis**
A. R. ALLEN, G. E. MARCY, and J. K. YU. *Diseases of the Chest* [*Dis. Chest*] **26**, 41–46, July, 1954. 4 refs.

The authors analyse the results in 101 cases of tuberculosis treated at the Central Washington Tuberculosis Hospital, Selah, Washington, with a combination of three antituberculous drugs. In 9 cases the disease was extrapulmonary, involving the renal tract or bone. Adults received 1 g. of streptomycin twice a week, 10 g. of PAS daily, and isoniazid in a dosage of 4 mg. per kg. body weight. In children under 12 the dosage of streptomycin was 0·5 g. twice a week and that of PAS was adjusted to body weight; the drugs were administered for most of the time spent in hospital. At the time of writing 60 patients had been discharged from hospital after an average stay of 207 days, 36 were still in hospital, and 5 had died. While under treatment the patients were allowed to be ambulant as soon as possible, and after discharge were encouraged to return immediately to their previous occupations. None of the discharged patients showed any retrogression in a 6-month observation period.

In 20 of the cases surgical treatment, either resection or wedge resection plus decortication, was considered necessary in addition. In general the authors recommend surgical intervention: (1) when the patient's sputum has remained positive for 3 months in spite of the administration of antituberculous drugs; (2) when there are extensive localized areas of destruction of lung tissue; (3) when the patient seems unlikely to accept prolonged stay in hospital; and (4) when portions of the lung may be saved by decortication.

The toxic effects of the drugs varied. In 2 cases dermatitis followed the use of streptomycin, but cleared up when dihydrostreptomycin was substituted. Toxic nephritis occurred in 2 patients with renal involvement, and led to the withdrawal of streptomycin. PAS was discontinued in 4 cases because of fever, and isoniazid caused the recurrence of convulsions in a known epileptic. At the end of 3 months culture of the gastric contents for tubercle bacilli gave positive results in only 14 cases, and in all but 2 of these the cultures had become negative within 6 months when other debilitating factors were corrected. *L. Capper*

81. **Streptomycin Sensitivity of Tubercle Bacilli from Resected Lungs**
E. W. STERN and A. GOLDMAN. *Diseases of the Chest* [*Dis. Chest*] **25**, 601–610, June, 1954. 17 refs.

An investigation was carried out to determine whether the inflammatory reactions in tissue play any part in the development of resistance by tubercle bacilli to streptomycin. Preliminary work on sputum and gastric washings from 258 patients with chronic pulmonary tuberculosis showed that the development of resistance was directly proportional to the total amount of streptomycin administered, and that this resistance was delayed when streptomycin was combined with PAS.

At the City of Hope Medical Center, Duarte, California, 124 specimens of tissue were obtained at pneumonectomy, lobectomy, or other operation from 33 patients, tubercle bacilli being cultured from the tissue, as well as from sputum and gastric washings collected before operation. In each case it was found that bacilli cultured from different types of lesion—for example, fibrotic, caseous, or cellular—had very much the same degree of sensitivity to streptomycin.

It is concluded that differences in the inflammatory reaction of the infected lung do not affect the development of streptomycin resistance by tubercle bacilli.
T. M. Pollock

82. **The Effect of Preoperative Streptomycin on the Incidence of Bronchopleural Fistula after Pulmonary Excision for Tuberculosis**
W. GORDON. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **28**, 1–3, July, 1954. 1 ref.

In this short paper the author produces figures which support the view that the incidence of broncho-pleural fistula after pulmonary resection for tuberculosis is reduced by the administration of streptomycin. In the series of 160 cases here reviewed, which were treated at hospitals near London, the administration of streptomycin for at least 3 weeks preoperatively resulted in a reduction in the incidence of broncho-pleural fistula from 24% to 6%. This improvement is attributed to the beneficial effect of streptomycin on the endobronchial tuberculous lesion which commonly develops at the site of bronchial section, and which is probably an important factor in the formation of fistulae. It is emphasized that the period of preoperative treatment with streptomycin should be at least 3 weeks, shorter periods having been found ineffectual.

[The high over-all fistula rate in this series is accounted for by the fact that all cases in which middle or lower

lobe excision was performed (and in which no fistulae occurred) were excluded from the study.]

A. M. Macarthur

83. **The Effect of Incomplete Pneumothorax of Short Duration on Tuberculous Cavities.** (Über die Wirkung kurzdauernd geführter, unvollständiger Pneumothoraces auf tuberkulöse Lungenkavernen)

H. NAGORNY. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **112**, 32–52, 1954. 16 figs., 26 refs.

The author has analysed the effect of unsuccessful pneumothorax, which was maintained for only a short time, on the cavitary lesions in 103 tuberculous patients under treatment at Oderberg Sanatorium, St. Andreasberg im Harz, Germany. In 72 cases only one cavity was present at the beginning of treatment; in 16 (22%) of these the cavity closed after treatment, and in a further 22 (30%) it became smaller. In 8 of these last cases the cavity closed later, so that cavity closure occurred in altogether about one-third of the cases, a result which the author believes to have been due to the partial pneumothorax. In 24 cases (33%) the cavity remained unchanged and in 10 cases (14%) it increased in size; only cavities with a diameter of 2 cm. or less were favourably influenced. The other 31 patients, who had multiple cavities, were not benefited. The author claims that it became evident in the first 2 to 4 weeks of treatment in which cases partial pneumothorax would be effective in promoting cavity closure.

[In the absence of controls it would be unwise to assume that the pneumothorax in these cases had any influence on the course of the disease.] *John Lorber*

84. **Suture Ligation of the Lung and Partial Thoracoplasty in the Treatment of Tuberculosis. A Four-year Experience**

P. T. DE CAMP and P. W. ACREE. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 61–70, July, 1954. **10** figs., 4 refs.

The results of 4 years' experience at the Charity Hospital and Ochsner Clinic, New Orleans, of the Paulino procedure for the treatment of pulmonary tuberculosis are described. The technique consists in suture ligation of the diseased upper lobe with three or more encircling crochet-cotton ligatures, combined with a small one-stage thoracoplasty conserving the first rib. The advantages claimed for it include conservation of lung function, absence of deformity, and completion in one stage. The operation was performed 42 times on 38 patients, many of whom had advanced or bilateral tuberculosis. There were 3 deaths, caused by pulmonary embolism, respiratory insufficiency, and massive pulmonary haemorrhage respectively; the last of these, which was not confirmed by necropsy, was thought to originate from the contralateral lung. Other complications included 2 cases of infection of the extra-pleural space and one of empyema, none of these infections being tuberculous. There has been no opportunity for pathological study of the constricted upper lobes following ligation.

A review of these cases at least 11 months after operation showed that in 29 cases the tuberculosis was inactive, while 5 patients still had active disease and 3 were dead. *S. F. Stephenson*

85. **The After-history of Pulmonary Tuberculosis. III. Minimal Tuberculosis**

N. S. LINCOLN, E. B. BOSWORTH, and D. W. ALLING. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 15–31, July, 1954. 6 figs., 11 refs.

The authors analyse the histories of 448 patients who were diagnosed, at the Hermann M. Biggs Memorial Hospital, Ithaca, New York, as having minimal pulmonary tuberculosis during the years 1937 to 1947 and who were followed up at yearly intervals until 1951. Of these patients, 134 were considered to have active disease at the time of the diagnosis and in the remaining 314 the disease was considered to be inactive. Of these latter, after 10 years approximately one-eighth had either died of tuberculosis or had active disease, the active disease in all cases resulting from a relapse. The deaths mostly occurred in the later years of observation and the death rate did not exceed the expected mortality.

Among the other 134 cases there was a rapid decrease in the percentage of active cases during the first 3 years, suggesting that there is a strong tendency for active minimal tuberculosis to become arrested; after this period, however, there was little change in the status of the disease. Deaths occurred during the first year of observation and continued throughout the period; about one-fifth of the patients had active disease or had died from tuberculosis 10 years later. There were 14 deaths in this group during the 10-year period, a figure which significantly exceeds the expected mortality. This group was subdivided into (*a*) 62 patients who were admitted to hospital within 3 months of diagnosis, and (*b*) 72 who were not treated in hospital. The clinical course in these two subgroups was very similar, but the authors consider that this should not be interpreted as disproving the value of rest in bed, and probably shows only that the method of analysis was not adequate.

In the whole series the relapse rate during any one year declined as the number of years of uninterrupted arrest increased, but on the other hand the remission rate declined as the number of years of uninterrupted active disease increased. *G. M. Little*

86. **Tuberculosis and Abortion**

G. SCHAEFER, R. G. DOUGLAS, and I. H. DREISHPOON. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 49–60, July, 1954. 7 refs.

Of 665 patients with tuberculosis admitted to the New York Lying-in Hospital between September, 1932, and January, 1952, 565 had full-term or premature deliveries, 66 were subjected to therapeutic abortion, and 34 had a spontaneous abortion. Thus nearly 10% of patients admitted to the hospital with tuberculosis during this 20-year period underwent therapeutic abortion. But from 1932 to 1937 the figure was 23%, whereas in the period 1948–51 it had decreased to 3·7% and the figure has declined even farther during the past few

years. At the present time tuberculosis is rarely an indication for therapeutic abortion.

Many of the patients in whom therapeutic abortion had been performed were lost to follow-up, largely because they discharged themselves from hospital soon after the operation in the belief that this had cured their tuberculosis. However, 39 were traced and of these 15 were judged to have active tuberculosis and 24 inactive disease. Of the former, 2 (13%) were improved, 7 were unchanged, in 5 the disease had progressed, and one had died. Of the latter, none was improved, 21 were unchanged, in one the disease had become active, and 2 patients had died.

The 34 spontaneous abortions which occurred represent an incidence of 5% of all patients admitted with tuberculosis during the period reviewed. The incidence of spontaneous abortion in non-tuberculous patients during the same period was 9%, thus suggesting that tuberculosis *per se* was not a factor in spontaneous abortion. At follow-up 3 of the 34 patients had active disease, which was fatal in one case and unchanged in the other 2. In the 29 patients with inactive disease, this remained unchanged in every instance.

Of the 565 patients who had full-term or premature deliveries, 461 were followed up. Of the 66 with active disease, 37 (56%) were improved, 25 unchanged, in 2 the disease had progressed, and 2 had died. The 395 patients with inactive disease showed an improvement in 6 cases, no change in 380, activation of the disease in 9 cases, but no deaths. Thus only 13% of patients with active disease on whom therapeutic abortion was performed experienced improvement of the tuberculosis, compared with 56% who improved after full-term or premature delivery. In those with inactive tuberculosis there was no significant difference between those who underwent abortion and those delivered naturally. The authors conclude, therefore, that in the majority of patients suffering from tuberculosis therapeutic abortion is not indicated, but suggest that each case should be considered individually. *G. M. Little*

EXTRA-RESPIRATORY TUBERCULOSIS

87. **Blood Changes Associated with Disseminated Tuberculosis. Report of Four Fatal Cases and Review**
J. R. FOUNTAIN. *British Medical Journal* [*Brit. med. J.*] **2**, 76–79, July 10, 1954. 12 refs.

In this paper from the General Infirmary at Leeds severe haematological changes in 4 patients, aged 22 to 61, with generalized tuberculosis are described. Haemoglobin values ranged from 32 to 60% (Haldane), and in all 4 cases macrocytosis was a feature. Leucopenia was generally present. In 2 cases the anaemia was of the leuco-erythroblastic type. Examination of the bone marrow in 3 cases revealed depression of the blood-forming elements with a preponderance of lymphocytes. At necropsy in one case aleukaemic lymphatic leukaemia with generalized tuberculosis was observed.

The author stresses the difficulty of diagnosis in these cases, and suggests that when pancytopenia, with or without depression of the blood-forming elements of the bone marrow, is accompanied by pyrexia and loss of weight a diagnosis of tuberculosis should be considered. In addition to routine diagnostic procedures lymph-node biopsy should be carried out and the bone marrow examined for miliary tuberculous foci. Blood obtained at marrow biopsy should be cultured and used for guinea-pig inoculation. *D. G. Adamson*

88. **The Manifestations, Limits, and Evolution of "Cold" Miliary Tuberculosis.** (Aspects, limites et destin de la granulie froide)
J. VIDAL and C. GAILLARD. *Presse médicale* [*Presse méd.*] **62**, 1109–1112, July 31, 1954. 9 refs.

In the authors' experience "cold" miliary tuberculosis is a relatively rare occurrence and is the most benign form of chronic tuberculosis. Among the patients attending the Tuberculosis Clinic of the Montpellier Faculty of Medicine they have collected only 25 cases, representing 1·5% of the total, during the last 15 years. The radiological appearance is of diffusely distributed, small nodules, and differs from that of tuberculous bronchopneumonia or an infiltrative process. Coexistent infraclavicular cavities are found in about 60% of cases. The clinical picture is characterized by loss of weight, fatigue, normal temperature, and cough with or without sputum, in which tubercle bacilli are not always present. The authors describe three forms of cold miliary tuberculosis—a unilateral form, a mixed form (consisting in miliary tuberculosis in one lung and an infiltrative process in the other), and an atypical form (in which the nodules tend to be larger and unequal in size); this third form occupies an intermediate position between miliary and bronchopneumonic tuberculosis.

They also discuss three methods of treatment—with rest and diet alone, with chemotherapy, and with collapse therapy. The first method was adopted in only 3 of their cases, and was initially successful after 6 to 40 months in that the micronodular radiographic appearance resolved. In 2 cases, however, there was a subsequent relapse. In 17 cases streptomycin was used, alone or together with PAS, sulphones, and isoniazid in various combinations, with clearance of the nodules in 10 out of the 13 in which adequate time has elapsed for the effect to be judged, cavities also disappearing in 3 cases; however, relapse occurred in half these cases. Collapse therapy was employed in cases of residual cavitation after chemotherapy and in 5 cases from the start. In the latter it was initially successful, but a subsequent relapse, with cavitation of the opposite lung, occurred in every case. Altogether relapse occurred within 4 years in 72% of those cases responding initially, the recurrent disease always taking the fibrocaseous form. *Franz Heimann*

89. **Partial Nephrectomy for Tuberculosis of the Kidney. Conservative Treatment—Operation. A Case of Heminephrectomy.** [In English]
A. STEINBOCK. *Annales chirurgiae et gynaecologiae Fenniae* [*Ann. Chir. Gynaec. Fenn.*] **43**, Suppl. 4, 1–44, 1954. 30 figs., 34 refs.

Venereal Diseases

90. **The Treatment of Chancroid Infection. A Report of Twenty-five Cases**
J. A. PAPARELLA. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 345–348, July, 1954. 2 figs., 3 refs.

The results of chemotherapy in 25 proved cases of chancroid infection are reported. In all the cases smears were cultured, *Haemophilus ducreyi* being isolated in 17 instances. Bubo formation was seen in 11 cases, including 5 in which culture was negative. None of the patients developed syphilis.

Aureomycin alone was given to 12 of the patients, a combination of aureomycin and sulphadiazine to 5, streptomycin and sulphadiazine to 5, aureomycin and streptomycin to 2, and streptomycin alone to one. The dosage of aureomycin was 1 g. initially and 250 to 500 mg. every 6 hours for 3 to 5 days.

Satisfactory results were obtained with aureomycin alone, no added benefit being observed when aureomycin in combination with other antibiotics or with sulphadiazine was given. Ulcers healed in 4 to 7 days after the start of treatment, adenopathy disappearing after a somewhat longer period.

The author admits that aureomycin may mask the early signs of syphilis or lengthen the incubation period, and suggests that serological tests for syphilis should be carried out for 3 to 5 months after treatment with aureomycin ceases. [This is an easy matter in military practice, but is a considerable drawback to the use of aureomycin in civilian practice or where supervision for 3 to 5 months is not possible.] *Robert Lees*

91. **Investigations into the Pathogenicity of Pleuropneumonia-like Organisms in the Urogenital Tract in Man, with Special Reference to Non-specific Urethritis.** (Untersuchungen zur Pathogenität der pleuropneumonieähnlichen Organismen im Urogenitaltrakt des Menschen mit besonderer Berücksichtigung der unspezifischen Urethritis)
H. RÖCKL, T. NASEMANN, and E. STETTWIESER. *Hautarzt* [*Hautarzt*] **5**, 340–348, August, 1954. 8 figs., bibliography.

At the University Dermatological Clinic, Munich, examination of the urogenital secretions of 443 patients for the presence of pleuropneumonia-like organisms (P.P.L.O.) gave the following results. Of 115 specimens from men who had never had any urogenital disease, 22 (19·1%) gave a positive culture, and of 120 specimens from men with non-specific urethritis, 32 (27%) were positive. Of 20 cases of chronic prostatitis, the prostatic secretions were positive for P.P.L.O. in 3 (15%). Culture of cervical or urethral scrapings from 117 apparently healthy women was positive for P.P.L.O. in 73 instances (62%), and of 31 urethral specimens from healthy children of both sexes, 4 were positive.

The authors point out that the difference between the results in men with non-specific urethritis and those in controls is insignificant, and from these as well as the other findings they conclude that P.P.L.O. are normal inhabitants of the urogenital tract. The possibility of the organisms assuming pathogenicity at certain times, however, is not altogether dismissed.

G. W. Csonka

SYPHILIS

92. **The Value of Merthiolated Sera in Evaluation Surveys**
C. R. REIN and L. C. KELCEC. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 308–312, July, 1954. 8 refs.

" Merthiolate " (sodium ethylmercurithiosalicylate) is an excellent bacteriostatic and bactericidal agent for the preservation of sera. It has been found to be of value in evaluating serodiagnostic tests for syphilis. It is also of value in preparation of positive control sera and for the shipment of sera from distant places to a central laboratory for serologic testing.—[Authors' summary.]

93. **Three Years' Practical Experience of the Treponemal Immobilization Test (Nelson and Mayer's Method).** (Trois années de pratique du test d'immobilisation du *Treponema pallidum* (méthode de Nelson et Mayer))
A. VAISMAN, A. HAMELIN, and H. VAISMAN. *Presse médicale* [*Presse méd.*] **62**, 1074–1075, July 17, 1954. 23 refs.

The authors discuss the practical aspects of the *Treponema pallidum* immobilization (T.P.I.) test on the basis of their experience in the performance of 7,922 tests at the Alfred-Fournier Institute, Paris, during 1951–3.

In seronegative primary syphilis the T.P.I. test result was invariably negative before treatment, but in the majority of cases became positive later, this positivity persisting in some instances up to 18 months in spite of negative results of standard tests and of adequate treatment. In seropositive primary cases and in secondary cases the T.P.I. reaction became positive later than did other reactions and remained so for much longer. It is suggested that the performance of this test after several years might prove useful in confirming the efficacy of treatment.

In cases of clinical tertiary syphilis, asymptomatic latent syphilis, and cases insufficiently or irregularly treated, as well as in those in which there was clinical or serological relapse, the T.P.I. reaction was invariably positive and remained so after the other reactions had become negative as the result of treatment. Similar results were obtained in tests of both blood and cerebro-

spinal fluid in cases of tabes dorsalis and general paresis. The reaction was also positive in all cases of congenital syphilis. Attention is drawn, however, to the possibility of a passive transfer of antibodies from a serologically-positive mother in neonatal cases giving a positive reaction which subsequently becomes negative.

Of the 7,922 samples of serum examined 265 (3·35%) were considered to have given false positive reactions to the standard tests, these reactions being feeble or variable as a rule. In cases of re-infection formation of antibodies was more rapid than in first infections and the T.P.I. reaction became positive earlier. The authors claim that a positive T.P.I. reaction is the most reliable evidence of the presence of a recent or old syphilitic infection, antibodies never having been found in normal subjects or in any disease other than the treponematoses. Because of the long duration of positivity the T.P.I. test allows of retrospective diagnosis of syphilis in treated cases, and a negative test result after treatment is probably the most reliable criterion of cure. They point out that the persistence of immobilizing antibodies does not necessarily indicate active disease.

Benjamin Schwartz

94. **Comparative Reactivity of the VDRL Slide and Other Tests for Syphilis in Random Population Groups (Including *Treponema pallidum* Immobilization Test)**
A. HARRIS, S. OLANSKY, and H. N. BOSSAK. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 295–303, July, 1954. 14 refs.

From 19,591 blood specimens collected from volunteer donors, 2,560 random samples were tested for syphilis at the Venereal Disease Research Laboratory of the U.S. Public Health Service by 4 slide microflocculation methods using cardiolipin-type antigens, namely, the V.D.R.L. slide, Kline standard, Rein–Bossak, and Mazzini tests. In 52 cases the results were not in agreement and the residual serum from these specimens was subjected to the *Treponema pallidum* immobilization (T.P.I.) test. A direct comparison of the V.D.R.L. slide and T.P.I. tests was also made on 466 specimens.

The results of these comparisons [which are well tabulated] suggest: (1) that the V.D.R.L. slide test is rather less sensitive than the other three serum tests; (2) that a positive result in the T.P.I. test combined with a negative result in the V.D.R.L. slide test is probably a more frequent discrepancy than the reverse; and (3) that not one of the five tests used supported the clinical findings or the history in 100% of cases.

G. L. M. McElligott

95. **The Anticomplementary Reaction in Syphilis Serodiagnosis**
A. GELPERIN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 304–307, July, 1954. 10 refs.

The phenomenon of the anti-complementary reaction in complement-fixation tests is neither absolutely preventable nor completely understood. From investigations carried out by the authors at Johns Hopkins University and Hospital, however, it is evident that positive serum is made anti-complementary by the addition of the alcoholic extract of normal human serum. Eagle's routine Wassermann technique revealed no haemolytic factors, nor were the prepared antigens in themselves anti-complementary. The author's experiments also indicate that while benzene has no effect, the addition of ether makes serum lipids "available" as antigen, cholesterol merely acting as a "fortifying" agent. The author considers that syphilitic serum contains the ingredients necessary to complete an antigen–antibody reaction. He also assumes that the anti-complementary phenomenon may result from the mobilization of the serum lipids and their consequent availability as an antigen, and that this mobilization is in some way produced by treating the serum with ether.

G. L. M. McElligott

96. **Cardiolipin Antigen in the Kolmer–Wassermann Test for Syphilis**
S. J. KLEIN, B. E. KONWALER, and G. M. LEIBY. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 318–329, July, 1954. 31 refs.

In this article the authors record a comparison of cardiolipin antigen with standard Kolmer antigen in the Kolmer–Wassermann reaction. Parallel testing was carried out on 374 sera from known cases of syphilis, on 518 presumed non-syphilitic sera, and on 2,956 unclassified sera. Though cardiolipin antigen gave a significantly higher incidence of false positive reactions in the non-syphilitic sera, in general it gave results which correlated better with a history of syphilis, especially in low titre, than the Kolmer antigen. This was also the case in the unclassified sera.

The results of a large-scale screening of 40,010 unclassified sera with the Kline and Kahn tests are also reported. These showed the more sensitive Kline test to be more efficient for screening purposes than the Kahn test in spite of the latter being more specific.

G. L. M. McElligott

97. **Experience with the Cardiolipin Complement-fixation Reaction. I. Analysis of the Results of 62,910 Serological Tests for Syphilis.** (Erfahrungen mit der Cardiolipin-Komplementbindungsreaktion. 1. Auswertung der Ergebnisse von 62910 serologischen Luesuntersuchungen)
F. LEGLER. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **140**, 87–99, 1954. Bibliography.

Between 1950 and 1953, 62,910 sera were examined for syphilis at the State Bacteriological Research Institute, Erlangen, 7 different tests being employed. These were the cardiolipin–complement-binding reaction (C.C.B.R.) (using cardiolipin as antigen), three types of the Wassermann reaction (with syphilitic liver, human heart, and calf heart extract as antigens), the "citochol" reaction, the Meinicke II test, and the Kahn test. The greatest number of strongly positive results were obtained with the cardiolipin test (Kolmer technique), followed in order by the Meinicke II test, the citochol reaction, and the Kahn test. The C.C.B.R. was alone positive in 2,244 samples of serum, most of which came from old,

treated cases, whereas the Wassermann reaction using the other antigens, was alone positive in 949 cases, most of which, however, were thought to be non-syphilitic.

G. W. Csonka

98. **The Relation between the Quantitative Kahn and Wassermann Reactions and the Erythrocyte Sedimentation Rate.** (Das Verhalten von quantitativer Kahn- und Wassermann-Reaktion und Blutkörperchensenkungsgeschwindigkeit)

W. KITTSTEINER. *Archiv für Dermatologie und Syphilis* [*Arch. Derm. Syph. (Berl.)*] **198**, 23–30, 1954. 5 figs., 5 refs.

Investigation into the cause of the well-known variability of the titre in serial serological tests for syphilis on individual patients, even when laboratory techniques, reagents, and treatment are kept as constant as possible, suggested that there was some correlation between the titre and the erythrocyte sedimentation rate (E.S.R.). This was proved to be statistically significant for the Kahn and Wassermann reactions and to be of particular importance in cases in which the E.S.R. is either very low or very high. Some examples, with statistical evaluation, are given.

[This is an interesting line of research. It is not clear from the paper whether the abnormal E.S.R. was thought to be due to syphilis or to other causes.]

G. W. Csonka

99. **Results of Penicillin, Cortisone, and Non-penicillin Treatment of Syphilitic Optic Atrophy, with Report of Clinical Observations**

J. V. KLAUDER and B. A. GROSS. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 270–287, July, 1954. 11 refs.

This paper reports 104 cases of syphilitic optic atrophy (99 due to acquired and 5 due to congenital syphilis) treated with penicillin, alone or together with other measures, and compares the results with those in 86 patients treated before penicillin was available.

The first group of 39 patients received 4·2 mega units of aqueous penicillin alone, and the same course was given together with fever and metallotherapy to patients requiring retreatment. Favourable progress was noted in 26 cases, while the condition worsened in 13, retreatment being given in 7 instances. Before treatment the condition was considered to be progressive in 34 of these patients.

The second group consisted of 29 patients, in all of whom the optic atrophy was considered to be progressive. They were given 6 mega units of penicillin and 16 of them also received fever therapy (malaria or typhoid vaccine). A favourable response was noted in 18 cases, while the optic atrophy progressed in 11; retreatment was given to 6 patients. A third group of 36 patients with progressive optic atrophy were given 11 mega units of penicillin, 14 receiving fever therapy in addition. Metal chemotherapy, more penicillin, and in some instances cortisone or ACTH were given on retreatment. A favourable outcome was noted in 23 cases, while progress was unfavourable in 13, 8 of which were retreated.

The 86 patients in the " non-penicillin " group received a variety of forms of treatment, including arsenic and bismuth, and in some cases fever and subdural treatment. Favourable progress was recorded in 36 cases, while in 50 the condition progressed.

[The variations in the regimen of treatment given in the four groups make any form of strict comparison extremely difficult. This paper, however, represents the fruits of a life-time of experience and as such must command respect.]

R. R. Willcox

100. **Penicillin Treatment of General Paresis. A Clinicoanatomic Study**

A. J. GIANASCOL, G. D. WEICKHARDT, and M. A. NEUMANN. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 251–269, July, 1954. 6 figs., 9 refs.

The clinical and necropsy findings (including the histology of the brain) in 14 patients suffering from general paresis who had received only 6 mega units of aqueous sodium penicillin within a period of 30 days are reported. It is concluded that this dose was adequate to arrest the pathological process of general paresis, any residual lesions being attributable to changes such as neurone destruction which probably anteceded treatment. The microscopical findings included persistence of meningeal fibrosis with minimal lymphocytic and plasma-cell infiltration, persistence of a prominent marginal gliosis, persisting evidence of cortical neurone loss, and in many cases minimal to moderate disturbance of the architecture of the cortex. Astrocytosis and microglial reaction, including the presence of rod cells, may apparently persist to a slight, and less frequently to a moderate, degree. As the interval between treatment and death lengthened perivascular infiltration gradually subsided and the neuropathological findings approached those of inactive paresis until, after 38 months, there were no signs of activity of the syphilitic process in the brain.

R. R. Willcox

101. **Treatment of Early Syphilis with Chloromycetin**

M. A. MAZZINI and A. A. BLASI. *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **38**, 341–344, July, 1954. 7 refs.

The authors report, from the University of Buenos Aires School of Medicine, the results of the treatment with chloramphenicol of 9 patients with early syphilis. In 4 cases the drug was given in daily oral doses ranging from 40 to 65 mg. per kg. body weight, and in 6 cases (one patient was re-treated for reinfection) in doses of 75 to 100 mg. per kg., treatment being continued for 6 to 8 days. The surface lesions healed rapidly in all cases in the latter group, but of the 4 cases receiving the lower dosage, healing was delayed in 3. Serological reversal appeared to be satisfactory. The drug was well tolerated in spite of the high dosage, which the authors advise for the type of syphilis encountered in Argentina. [Most British doctors would hesitate to use the high dosage of chloramphenicol advocated, but such treatment might be helpful when the patient is intolerant of penicillin.]

Robert Lees

Tropical Medicine

102. **The Treatment of Amebiasis with PAA-701—a Preliminary Report**
H. BARRIOS. *Gastroenterology* [*Gastroenterology*] **27**, 81–86, July, 1954. 7 refs.

The synthetic compound PAA-701 is diallyl-diethyl-aminoethyl phenol dihydrochloride and contains no iodine or arsenic in its molecule. *In vitro* it has been shown to kill amoebae in dilutions as high as 1 in 50,000. At the Santa Rosa Military Hospital, Iquitox, Peru, 20 adult patients with acute amoebic dysentery were treated with the drug and followed up with monthly examinations for 6 months. The dosage was 0·5 g. 3 times daily until the stools were free from amoebae and sigmoidoscopic examination showed healing of the ulcers, the total dose ranging from 7·5 to 56 g. but in most cases being between 10 and 18 g. In 4 cases 2 g. was given daily without causing any toxic effects.

The acute symptoms were rapidly controlled, usually within 2 days. Trophozoites of the amoebae in the stools disappeared in 3 to 22 days (average 7 days), and the ulcers in the colon healed in 5 to 25 days (average 10 days). One patient, who had suffered many relapses during 2 years and who had been resistant to treatment with fumagillin, responded well to PAA-701, amoebae disappearing from the stools by the 22nd day. In another case there was a hepatic lesion (as indicated by liver function tests) which was unchanged by PAA-701. In 17 of the cases there were no toxic effects from the drug, but in the other 3 there was slight anorexia, transitory albuminuria, and violent headache respectively. All the patients remained clear of infection during the subsequent follow-up period [which in 8 cases, however, lasted only 1 to 3 months]. The compound is recommended for the treatment of acute amoebic dysentery as being efficacious and non-toxic. *F. Hawking*

103. **Amebicidal Effects of Fumagillin *in vivo*; Preliminary Communication**
R. HERNANDEZ DE LA PORTILLA, E. BECERRA, and J. RUILOBA. *Gastroenterology* [*Gastroenterology*] **27**, 93–97, July, 1954. 4 refs.

At the Hospital for Nutritional Diseases, Mexico City, 7 patients with amoebic ulceration of the rectum or colon and trophozoites in the stools, one with cysts in the stools, and a ninth with an amoebic ulcer of the skin near the anus were treated with fumagillin in doses of 50 to 200 mg. per day for 9 to 14 days. Cure was obtained in all cases, the amoebae and the ulcers disappearing, but one patient developed dysentery and another showed cysts of *Entamoeba histolytica* in the stools 3 months later; it was not certain whether these 2 patients suffered from relapse or from re-infection. Side-effects were noted in 5 patients, 2 complaining of anorexia and insomnia and 3 developing urticaria, with desquamation of the skin of the hands. These untoward effects were mild and subsided quickly when treatment was stopped. Three patients received 200 mg. of the drug daily for 14 days without ill effect. Fumagillin is recommended as an effective and non-toxic drug for the treatment of amoebic dysentery. The authors suggest that the optimum dose is probably about 100 to 120 mg. daily for 10 days. *F. Hawking*

104. **The Distribution of the Sickle-cell Trait in East Africa and Elsewhere, and its Apparent Relationship to the Incidence of Subtertian Malaria**
A. C. ALLISON. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **48**, 312–318, July, 1954. 29 refs.

Sickling of the erythrocytes has until recently been presumed to be essentially a negroid phenomenon, but the discovery of sickle-cell anaemia in Greece and Italy and the great variations which have been shown to occur in the frequency of the sickle-cell trait between groups of individuals of apparently the same race, but living in different areas, have made it increasingly difficult to explain the distribution of the trait on racial grounds alone.

The author has recently obtained evidence indicating that persons with the sickle-cell trait possess considerable natural resistance to subtertian malaria (*Brit. med. J.*, 1954, **1**, 290). If this is so it may be supposed that where subtertian malaria is hyperendemic more children with the trait will tend to survive compared with children without the trait, some of whom will be eliminated before they have been able to acquire an immunity to malaria. The severity of sickle-cell anaemia is such, however, that there is a high mortality among children homozygous for the trait and, according to the hypothesis propounded, in any community the proportion of individuals with the sickle-cell trait would be the result of a balance between the severity of the prevailing malaria and the rate of elimination of the sickling gene in persons dying of the anaemia. Thus the incidence of the trait should be highest where subtertian malaria is hyperendemic.

In order to test this hypothesis over 4,600 Africans from 35 different tribes living in widely different environments in East Africa were examined for the sickling trait. Among groups of subjects of the same race from different areas there was a striking correlation between the severity of malaria in the area and the frequency of the sickling trait. Amongst the Bantu, for example, no case of sickling was found in 213 individuals tested at Mashakos, where endemic subtertian malaria does not exist, whereas sickling was found in 40·5% of 126 individuals tested at Musoma, Kanesi, where malaria is hyperendemic. All tribes coming from regions where malaria is hyperendemic showed an incidence of the trait of more than 10%, whereas in tribes coming from areas where malaria is absent or epidemic the incidence was less than 10%. *W. H. Horner Andrews*

Nutrition and Metabolism

105. **Treatment of Pellagra with Corticotrophin (ACTH).** (Notre expérience du traitement de la pellagre par l'hormone hypophysaire corticotrope (A.C.T.H.)
D. K. Miowski and I. S. Tadzer. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **81**, 259–270, May–June, 1954. 4 figs., 23 refs.

A clinical and laboratory investigation of 15 cases of severe pellagra at the Dermatological Clinic of the University of Skopje, Yugoslavia, suggested a relationship between the manifestations of the disease and adrenal dysfunction. Five severe cases were therefore treated with injections of 25 mg. of ACTH (corticotrophin) daily for 16 to 20 days without any other medication or change of diet. Improvement in the mental state, the condition of the skin, and the gastrointestinal symptoms was manifest in every case after 6 doses, and after 10 the patients were normal in every respect except for some residual skin lesions. After 400 to 500 mg. of ACTH had been given the patients were discharged cured, the only remaining sign of the disease being slight depigmentation of the skin in the areas which had been most severely affected.

James Marshall

106. **Dietary Supplementation of Vitamin B_{12} in Prepuberty School-age Children. I. Growth Studies**
J. W. Larcomb, C. S. Perry, and R. A. Peterman. *Journal of Pediatrics* [*J. Pediat.*] **45**, 70–74, July, 1954. 7 refs.

A series of studies of the effects of supplementation of the diet of children with vitamin B_{12} (cyanocobalamin) have been carried out by the authors on approximately 500 children aged 6 to 17 years living in the Ohio State Schools for the Deaf and the Blind, who were divided into an experimental and a control group by taking alternate names from the school roster. The present paper, however, is concerned only with those children who at the end of the period of study were less than 10 years old, and who had not suffered from serious illness during that time. These numbered 132, 60 being in the test group and 72 in the control group. All were given an adequate diet together with a multiple vitamin preparation containing 1 μg. of vitamin B_{12} daily. The experimental group received in addition 20 μg. of vitamin B_{12} by mouth daily, while the control children received a placebo.

The trial extended over 8 months, at the end of which time the test group had gained an average of $4{\cdot}50 \pm 0{\cdot}53$ lb. ($2{\cdot}04 \pm 0{\cdot}24$ kg.) and the controls $3{\cdot}80 \pm 0{\cdot}48$ lb. ($1{\cdot}74 \pm 0{\cdot}22$ kg.). The difference in favour of the experimental group was $0{\cdot}71 \pm 0{\cdot}072$ lb. ($0{\cdot}32 \pm 0{\cdot}033$ kg.), which is not significant according to standard methods of statistical analysis. However, when the results for underweight, normal, and overweight children were analysed separately, statistically significant differences in favour of the experimental group became apparent in respect of weight in the underweight group, and of weight (not highly significant) and height in the overweight group, no difference being found between treated and untreated normal children. These findings are considered to confirm the reports of other workers that vitamin B_{12} increases the weight of the underweight child, and it is suggested that the effect demonstrated on the height of the overweight child indicates that vitamin B_{12} " plays a role in some fundamental metabolic growth-regulating mechanism ".

[It is quite impossible to assess this report critically. The only quantitative data in the whole paper are those quoted in the abstract.] *John Yudkin*

107. **Body Sodium and Potassium. I. Simultaneous Measurement of Exchangeable Sodium and Potassium in Man by Isotope Dilution**
A. H. James, L. Brooks, I. S. Edelman, J. M. Olney, and F. D. Moore. *Metabolism* [*Metabolism*] **3**, 313–323, July, 1954. 19 refs.

In this paper from Harvard Medical School, Boston, the authors describe an isotope-dilution method for the simultaneous determination of exchangeable sodium and potassium levels in the human body. A double tracer technique, using radioactive sodium (^{24}Na) and radioactive potassium (^{42}K), is employed and the isotope mixture is separated chemically in the equilibration serum sample; in urine the tracers are estimated either by chemical separation or by a counting technique involving differential absorption by aluminium. It is claimed that the method compares favourably with that using a single isotope. *F. W. Chattaway*

108. **Body Sodium and Potassium. II. A Comparison of Metabolic Balance and Isotope Dilution Methods of Study**
G. M. Wilson, J. M. Olney, L. Brooks, J. A. Myrden, M. R. Ball, and F. D. Moore. *Metabolism* [*Metabolism*] **3**, 324–333, July, 1954. 11 refs.

At the Peter Bent Brigham Hospital (Harvard Medical School), Boston, the changes in body content of sodium and potassium have been studied in 16 patients both by metabolic balance studies and by the isotope-dilution method described above [see Abstract 107]; the differences between total exchangeable sodium and potassium measurements made at intervals were also compared with the cumulative balance totals over the same periods. In 33 out of the 39 paired results there was agreement within 125 mEq.

In most of the patients (all but one of whom had undergone surgical operation or suffered severe trauma such as burns) there was a loss of weight and of potassium and a gain of sodium during their stay in hospital. The results by the balance method showed a slightly

greater retention of sodium and potassium than did those by the isotope method, but in short-term studies this was of a low significance for sodium and was not significant for potassium. The considerable advantages of the isotope-dilution method over the balance-study method are indicated. *F. W. Chattaway*

109. **Absorption of Iron from the Gastrointestinal Tract**
W. J. GRACE, R. K. DOIG, and H. G. WOLFF. *Journal of Clinical Nutrition* [*J. clin. Nutr.*] **2**, 162–167, May–June, 1954. 2 figs., 21 refs.

In a study of the absorption of iron from the gastrointestinal tract carried out at the New York Hospital–Cornell Medical Center, New York, 2 mg. of iron per kg. body weight was given by mouth to 7 healthy fasting subjects and to one patient with a large gastric fistula. The serum iron concentration was determined hourly, and in the case of the patient the *p*H of the gastric juice was observed half-hourly. The same observations were repeated after 5 g. of sodium bicarbonate had been given with the iron.

It was found that ferrous ammonium sulphate raised the serum iron level to an average of 192 μg. per 100 ml., and ferric ammonium sulphate to a level of 166 μg. per 100 ml. after 2 hours—rises of 79 μg. and 53 μg. per 100 ml. respectively. The simultaneous administration of sodium bicarbonate did not influence the results. Similar results were noted when iron was given 3 hours after a meal to the subject with a gastric fistula. A gastric juice of *p*H ranging from 5 to 8 did not appear to impair absorption.

The authors conclude that the failure to absorb iron is due rather to lowered absorptive capacity of the upper small intestine than to a defect in hydrochloric acid secretion.

[These simple experiments confirm the accepted belief that the ferrous salt is better absorbed than the ferric, but the difference reported here is only just significant, and no more. It is an interesting speculation that the malabsorption of iron which accompanies achlorhydria is due not to the lack of acid resulting from atrophy of the gastric mucosa, but to changes lower down in the gastrointestinal tract, perhaps of a similar nature.]
Thomas B. Begg

110. **Fluid and Electrolyte Exchange in Patients with Burns**
J. P. BULL and N. W. J. ENGLAND. *Lancet* [*Lancet*] **2**, 9–17, July 3, 1954. 4 figs., 43 refs.

The intake and urinary output of fluid, sodium, potassium, and chloride in 33 patients treated for severe burns at Birmingham Accident Hospital were studied. The general pattern of response in these patients was similar to that described by Moore and Ball as "the metabolic response to surgery"—that is, retention of sodium and chloride and a moderate loss of potassium in the first few days after injury.

[For details of the findings the original paper should be consulted. The various problems presented by these observations are discussed in adequate detail.]
D. A. K. Black

METABOLIC DISORDERS

111. **Gas Transport Function of the Blood in Congenital Familial Methaemoglobinaemia**
A. G. BAIKIE and D. J. VALTIS. *British Medical Journal* [*Brit. med. J.*] **2**, 73–76, July 10, 1954. 4 figs., 18 refs.

The authors, working at the University and Royal Infirmary, Glasgow, have studied the blood oxygen dissociation curve in 2 cases of familial congenital methaemoglobinaemia in order to throw further light on the question whether this curve is shifted to the left, indicating an impaired release of oxygen to the tissues. Methaemoglobin was identified in the Hartridge reversion spectroscope by the presence of an absorption band at 630 mμ which disappeared on the addition of a few drops of 10% sodium cyanide. Methaemoglobin was estimated by a modification of the method of Evelyn and Malloy (*J. biol. Chem.*, 1938, **126**, 655) using an S.P. 600 spectrophotometer, and also by gas analysis, while total haemoglobin was estimated after conversion to cyanmethaemoglobin, as described by Evelyn and Malloy. Oxygen and carbon dioxide dissociation curves were obtained by the method described by Valtis and Kennedy (*Lancet*, 1954, **1**, 119), and the value I/K at different *p*H was determined from the Hill–Barcroft equation (taking n=2·5) by equilibrating the blood in tonometers at a standard oxygen pressure of 20 mm. Hg and at various pressures of CO_2. All values for CO_2 in the serum of whole blood were directly determined.

A shift to the left was found in both cases, but treatment with methylene blue restored the curve to normal. After treatment with ascorbic acid, however, it remained abnormal. The published results of similar studies, some of which are at variance with the authors' findings, are discussed. It is concluded either that there is more than one kind of congenital methaemoglobinaemia, or that the altered oxygen transport in this condition is due to some factor other than methaemoglobin itself.
D. G. Adamson

112. **Studies on the Effect of Probenecid ("Benemid") in Gout**
R. M. MASON. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 120–130, June, 1954. 5 figs., bibliography.

The effect of probenecid, a potent and non-toxic uricosuric agent, on the blood and urinary levels of uric acid in 7 patients with gout was studied at the West London Hospital. The patients had had gout for periods varying from 3 to 27 years, and the duration of the investigation was 7 to 86 days. Acute attacks of gout occurred during a control period and during treatment with probenecid. An increase in urinary excretion of uric acid was observed in gouty subjects as well as in healthy controls. The author's findings indicate that attacks of gout may occur in predisposed subjects in the presence of a normal serum uric acid level. He suggests, as a possible explanation of this phenomenon, that the paroxysms of gout may be due not to the uric acid *per se*, but to a precursor. *G. Loewi*

Gastroenterology

113. **Parotid Hypertrophy in Alcoholic Cirrhosis.** (La parotidose des cirrhoses alcooliques)
—. BONNIN. *Bulletin de l'Académie nationale de médecine* [*Bull Acad. nat. Méd. (Paris)*] **138**, 322–324, June 22, 1954.

The author claims that in 80% of cases of alcoholic cirrhosis of the liver there is enlargement of the parotid glands, and that this condition is also found in chronic alcoholics who have not developed cirrhosis. The enlargement is generally bilateral but not necessarily symmetrical. Although frequently unnoticed by the patient and often by the physician, the swelling is quite obvious when specifically sought. It is entirely painless and Stenson's duct is not affected. Histological and chemical investigations on biopsy and necropsy specimens show all the changes associated with progressive glandular overactivity, up to eventual exhaustion with mucous degeneration of the acini. The author believes that the parotid changes in these cases are similar to those in kwashiorkor and related syndromes of malnutrition.

T. A. A. Hunter

114. **Giant Hypertrophy of Gastric Mucosa. A Clinical and Pathological Study**
F. D. KENNEY, M. B. DOCKERTY, and J. M. WAUGH. *Cancer* [*Cancer (N.Y.)*] **7**, 671–681, July, 1954. 4 figs., 24 refs.

Giant hypertrophy of the gastric rugae is a rare condition which was first described by Menetrier in 1888 under the name of *polyadénomes en nappe* to distinguish it from *polyadénomes polypeux*, the more common type of glandular hypertrophy of the gastric mucosa. The condition is characterized by hypertrophy and hyperplasia involving the entire mucous membrane and forming a well-demarcated, thickened plaque composed of folds of mucosa so closely packed in rows that they resemble convolutions of the brain. The mucous membrane at the edge of the plaque is normal. The change may be localized or diffused.

In a study of the disease from the case records of the Mayo Clinic for the period 1926–51 only those cases, totalling 20, were accepted in which histological specimens were available, having been obtained at operation or, in one case only, at necropsy. No constant aetiological factor was present—indeed no cause at all was found in the majority of cases. In only 2 of the 20 cases was there evidence of moderate or excessive intake of alcohol. No occupational factor was noted. In the 3 cases with the most extensive lesions multiple adenomata of the endocrine system were also present. There were 13 men and 7 women, and 13 of the patients were in the fifth and sixth decades of life. Only 2 patients had no gastric symptoms, and in 11 cases the classic clinical picture of peptic ulcer was present, the remainder complaining of such symptoms as flatulence, nausea and vomiting, anorexia, and fullness after meals. Two patients reported haematemesis. The general condition of the patient was in most instances good and there was a striking lack of physical signs. The laboratory findings contributed little to the diagnosis.

The great similarity of the radiological appearances in giant hypertrophy of the gastric rugae to those of carcinoma and lymphosarcoma of the stomach is emphasized, but it is stated that there is a predilection towards involvement of the greater curvature in both the localized and diffuse forms. Microscopically, mucous cells, as well as chief and parietal cells, were well differentiated, in contrast to the findings in chronic gastritis. The lack of any tendency to undergo malignant change was noteworthy. The authors point out, however, that because of the unknown nature of giant hypertrophy of gastric rugae, the inconclusive nature of the symptoms and signs, and the resemblance to carcinoma in radiological appearance, surgical exploration is necessary for accurate diagnosis.

E. Forrai

115. **Primary Carcinoma of the Liver: Report of 20 Cases, including Two Treated with Triethylene Melamine**
H. M. WILSON. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 118–123, July, 1954. 8 refs.

Of 20 cases of primary carcinoma of the liver seen over a recent 10-year period at the Veterans Administration Hospital, Alexandria, Louisiana, 17 were confirmed at necropsy and 3 by liver biopsy. The incidence of primary carcinoma of the liver in the author's series was 2·58% in 657 [presumably consecutive] necropsies. Of the 20 patients 13 were negroes. There was associated cirrhosis in 10 out of the 20 cases, and the author points out that other workers have found the incidence of cirrhosis in similar cases to be 55 to 70%. He considers that a diagnosis of primary carcinoma of the liver should be seriously considered in the presence of rapidly progressive cirrhosis, pain in the epigastrium or right upper quadrant of the abdomen, weight loss and cachexia, and an enlarging liver, especially if the patient is a negro male. The failure of triethylene melamine (tretamine) in 2 cases and of nitrogen mustard in one to influence the outcome of the disease is recorded. [The paper contains no new findings.]

Thomas Hunt

116. **Hepatic Function after Operations for Portal Hypertension**
A. I. S. MACPHERSON, J. A. OWEN, and J. INNES. *Lancet* [*Lancet*] **2**, 356–361, Aug. 21, 1954. 8 figs., 27 refs.

The object of the investigation described in this paper from Edinburgh University was to discover whether surgical diversion of portal venous blood away from the liver in patients with portal hypertension leads to severe or permanent deterioration in liver function, as indicated

by biochemical changes, particularly in the concentration of plasma albumin and globulin.

In patients with chronic liver disease who were not subjected to surgery these values were shown to be relatively constant over short periods of time. In patients with liver disease any severe operation resulted in temporary deterioration in liver function, and portacaval anastomosis was not more prone to cause this than other operations of comparable magnitude. The degree and duration of the deterioration were determined mainly by the preoperative functional capacity of the liver. The difference between the results of liver function tests carried out before operation and the results of these tests a year or more after operation was slight and said not to be statistically significant, suggesting that no permanent deterioration in liver function had occurred as a result of operation. [Nevertheless, the figures given show a considerable rise in the average plasma globulin level a year or more after operation in patients subjected to portacaval anastomosis.] *P. C. Reynell*

117. **Some Observations on the Treatment of Ulcerative Colitis with A.C.T.H.**

A. P. Dick and A. G. Beckett. *British Medical Journal* [*Brit. med. J.*] **2**, 378–383, Aug. 14, 1954. 19 refs.

After reviewing the literature on the treatment of ulcerative colitis with cortisone or ACTH and on the complications encountered, the authors report an uncontrolled therapeutic trial of ACTH in 14 cases of this condition seen at Addenbrooke's Hospital, Cambridge. The hormone was given initially in a dosage of 15 mg. 6-hourly by intramuscular injection or 20 mg. daily in the form of a gel, this dosage being gradually increased until improvement, as judged by gain in weight and fall in temperature, was observed. The maximum effective dosage was continued for 2 to 5 weeks, and then gradually reduced. Details of the results and the duration of the follow-up are given in a comprehensive table, and certain cases are discussed.

In 7 of the 14 cases there was complete remission and in 4 some maintained improvement. The authors conclude that ACTH has a place in the management of cases of ulcerative colitis, particularly in acute and severe cases of recent onset. *J. Naish*

118. **Cortisone in Ulcerative Colitis. Preliminary Report on a Therapeutic Trial**

S. C. Truelove and L. J. Witts. *British Medical Journal* [*Brit. med. J.*] **2**, 375–378, Aug. 14, 1954. 2 figs., 12 refs.

A " blind " therapeutic trial of cortisone in ulcerative colitis was carried out at the Radcliffe Infirmary, Oxford, in conjunction with similar trials at hospitals in north-west London, Edinburgh, Leeds, and Birmingham, a total of 213 patients being treated. The dosage of cortisone was 100 mg. a day for the first 3 weeks, followed by smaller doses in the next 3 weeks. Approximately half of the patients received a placebo, but the physician in charge did not know whether the patient was receiving this or cortisone.

The results obtained in first attacks and in relapses are considered separately, the patient's condition being assessed as " clinical remission ", " improved ", and " no change or worse ". At the end of 6 weeks, in the series as a whole significantly more treated patients than controls were in clinical remission. Of the patients given cortisone during a first attack, 42% were in remission, 36% were improved, and only 22% showed no change or were worse. Of the patients given cortisone during second or subsequent attacks, the percentage in remission was slightly lower and the percentage improved was substantially lower than was the case in the patients treated during a first attack. The number of patients subjected to ileostomy and the number of deaths were higher in the controls than in the treated group. *X*-ray examination and sigmoidoscopy were not carried out in all cases, but such data as were available confirmed the general clinical assessment. A few patients had a relapse soon after cessation of cortisone therapy.

It is concluded that cortisone is beneficial in the treatment of an acute attack of ulcerative colitis.

J. Naish

119. **Roentgen Observations of the Ileostomy in Patients with Idiopathic Ulcerative Colitis. I. The Well Functioning Ileostomy**

F. G. Fleischner, P. Mandelstam, and B. M. Banks. *Radiology* [*Radiology*] **63**, 74–80, July, 1954. 2 figs., 9 refs.

In view of reports that ileal dysfunction has followed the operation of ileostomy in patients with idiopathic ulcerative colitis, the authors have carried out investigations at Beth Israel Hospital (Harvard Medical School), Boston, on 13 patients with a well-functioning ileostomy. In 2 of the cases ileostomy alone had been performed, in 3 cases ileostomy and partial colectomy, and in 8 ileostomy and total colectomy. The patients were studied both by noting the transit of barium given by mouth and after a barium enema through the ileostomy. For the enema examination a Foley catheter was passed into the stoma for 10 to 15 cm. and the balloon inflated with 15 ml. of air.

In all cases the width of the ileum proximal to the stoma was within normal limits, a finding which conflicts with that previously reported by other workers. Formed faecal matter was demonstrated in 3 of the cases, thus showing that the lower ileum was capable of inspissating its contents, and in no case was there any discharge of faecal matter through the catheter; this was in contrast to the observation that patients with dysfunction of the ileostomy commonly expel considerable amounts of ileal content when the catheter is inserted. The follow-through examination showed that the variations in transit time of the barium were similar to those found in normal subjects. In 2 of the cases there was some evidence of chronic ileitis, probably ulcerative, but in general all 13 patients showed good ileal function.

[This original investigation forms a useful foundation for the study of ileal dysfunction. The authors' promised report on the latter condition should prove to be of considerable interest.] *Sydney J. Hinds*

Cardiovascular System

120. **The Diagnostic Importance of the Blood Carbon Dioxide Content of Patients with Central Cyanosis**
M. M. PLATTS and W. WHITAKER. *American Heart Journal* [*Amer. Heart J.*] **48**, 77–81, July, 1954. 1 fig., 6 refs.

In an investigation carried out at the Royal and City General Hospitals, Sheffield, the carbon dioxide content of arterial blood was determined in 55 patients with central cyanosis, due in 16 cases to congenital heart disease and in the remainder to chronic bronchitis and emphysema with or without congestive heart failure. Taking the normal range as 44 to 52 volumes %, the arterial carbon dioxide content was below normal in most of those patients with congenital heart disease but without congestive heart failure, normal or raised in the majority of those patients with chronic bronchitis and emphysema but without heart failure, and invariably raised in those patients with congestive heart failure complicating chronic bronchitis and emphysema. It is concluded that the estimation of blood carbon dioxide content in patients with central cyanosis may be of diagnostic value. *A. I. Suchett-Kaye*

121. **Endomyocardial Fibrosis in Africa: Its Diagnosis, Distribution and Nature**
A. W. WILLIAMS, J. D. BALL, and J. N. P. DAVIES. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **48**, 290–311, July, 1954. 4 figs., bibliography.

From their experience at Mulago Hospital (Makerere College Medical School), Kampala, Uganda, the authors consider endomyocardial fibrosis to be one of the commonest causes of death from heart failure among Africans in this area. Analysis of a series of 231 necropsies on patients dying of heart failure showed that the four main causes were endomyocardial fibrosis, 33 cases (14·3%); renal hypertension, 37 (16%); syphilitic aortitis, 34 (14·7%); and rheumatic heart disease, 20 (8·7%). They do not consider it likely that the disease is peculiar to this small area of Africa, but attribute the comparatively high incidence here reported to the rise in the number of necropsies performed and the increased awareness of the condition at Kampala. Only fragmentary information is available on the incidence of endomyocardial fibrosis elsewhere; most of this is from Africa, but a few cases have been reported from the United States and from Europe.

Since in most cases only the end-results of endomyocardial fibrosis are seen, the nature of the onset and development of the condition are unknown. Post mortem, the left ventricle shows endo- and myocardial fibrosis and the posterior cusp of the mitral valve may be adherent to the ventricle wall. The right ventricular lesion usually produces obliteration of the cavity in the region of the apex, and occasionally the posterior cusp of the tricuspid valve becomes adherent to the ventricle. Clinically, these pathological changes result in left, right, or bilateral heart failure, with or without mitral incompetence or tricuspid incompetence. *X*-ray screening shows a large, globular heart shadow and greatly decreased pulsation, which is presumably due to poor myocardial contractility. Low-voltage electrocardiograms are common, but arrhythmia is rare.

The pathogenesis is largely speculative; two possible sequences are discussed, namely, endocardial damage leading to thrombosis followed by fibrosis, or subendocardial muscle injury resulting in endocardial thrombosis and again fibrosis. The roles of infection, allergy, malnutrition, and toxic agents as possible aetiological factors are considered. Of infection, the authors state that " the possibility of virus infection (by itself or with some other contributing factor) initiating a fibrosis–thrombosis or thrombosis–fibrosis cycle involving the inner layers of the heart wall cannot be dismissed ". In conclusion a plea is made for further information about the geographical and racial distribution of this condition, and the difficulties involved in studying the lesion in its early stages are emphasized. *J. Warwick Buckler*

122. **The P Wave in the Electrocardiogram in the Diagnosis of Heart Disease**
P. THOMAS and D. DEJONG. *British Heart Journal* [*Brit. Heart J.*] **16**, 241–254, July, 1954. 6 figs., bibliography.

From a detailed analysis of the P wave in the electrocardiograms of 100 normal subjects, made at the London Hospital using the three limb leads and Leads CR1, CR4, and CR7, criteria were established for the height and duration of the normal P wave, and the incidence of various patterns of P wave in the leads examined was determined. Small bifid P waves with prominence of the first peak were often found in Lead CR1 and never in CR7, whereas bifid waves with prominence of the second peak were sometimes found in CR7 but never in CR1.

Electrocardiograms from 245 patients with various types of heart disease were then reviewed in the same way and it was concluded that right atrial abnormality (as in cases of pulmonary stenosis or pulmonary hypertension) is associated with a P wave in Lead CR1 which is more than 2·5 mm. high and diphasic, pointed, or bifid with prominence of the first peak. On the other hand left atrial abnormality (as in mitral stenosis) is indicated when the P wave in CR4 or CR7 is more than 3 mm. high and bifid with prominence of the second peak, or when a peak-to-peak interval greater than 0·04 second occurs in a bifid wave in any lead. Patterns suggestive of combined atrial abnormality were identifiable in appropriate cases. It was also confirmed that the two atria are activated slightly asynchronously.
J. A. Cosh

123. **Ventricular Function. III. The Pathologic Physiology of Acute Cardiac Tamponade Studied by Means of Ventricular Function Curves**
J. P. ISAACS, E. BERGLUND, and S. J. SARNOFF. *American Heart Journal* [*Amer. Heart J.*] **48**, 66–76, July, 1954. 6 figs., 18 refs.

In further studies of ventricular function carried out at the Harvard School of Public Health, Boston, acute cardiac tamponade was produced in a number of dogs by injecting a known amount of air or saline into the pericardial sac, and the effect on cardiovascular haemodynamics determined. In particular, ventricular function curves (ventricular work plotted against effective filling pressure) were drawn up for different pressures in the pericardial space. The data presented confirm and help to explain the most important physiological consequence of tamponade, namely, restriction of cardiac output. This is due to the reduction in effective filling pressure owing to increased pressure in the pericardium and reduction of the pericardial space available for the diastolic expansion of the ventricles. The consequent shortening of diastolic ventricular muscle-fibre length results in less ventricular work. Since the pressure gradient across the veno-atrial orifice was less than 0·2 cm. H_2O both in the normal and tamponade states, there is no basis for the theory that the haemodynamic consequences of acute cardiac tamponade are due to obstruction of inflow.

Therapeutic considerations of interest to the clinician are also discussed. Thus artificial respiration by positive-pressure breathing should presumably be avoided, since it will increase the extrapericardial and therefore the intrapericardial pressure; alternating positive–negative pressure would be preferable, while in theory electrophrenic respiration should give optimum results. Similarly, since opening the chest will increase the mean pericardial pressure, pericardial aspiration should precede thoracotomy. Adrenaline increases the stroke work of the heart per unit of effective filling pressure and should be of value in the emergency of acute cardiac tamponade. *A. I. Suchett-Kaye*

124. **The Limits of Right Ventricular Compensation following Acute Increase in Pulmonary Circulatory Resistance**
A. C. GUYTON, A. W. LINDSEY, and J. J. GILLULY. *Circulation Research* [*Circulat. Res.*] **2**, 326–332, July, 1954. 5 figs., 11 refs.

Working at the University of Mississippi School of Medicine, the authors have studied the effect of partial occlusion of the pulmonary artery on various parts of the circulatory system in 29 dogs. At a preliminary operation a plastic tube was passed once round the pulmonary artery and the two ends brought through the chest wall, one anteriorly and the other posteriorly. By subsequent tension on the ends of the tube the pulmonary artery could be constricted. At the same time pressure measurements were made through a venous catheter and the cardiac output measured by the direct Fick method. In some cases, in order to eliminate reflex action, procaine (200 mg.) or piperocaine (150 mg.) was dissolved in 20 ml. of saline and injected into the spinal canal, artificial respiration and continuous infusion of adrenaline being given to keep these animals alive.

The findings, which are presented schematically as the algebraic average of the results, indicate that on constriction of the pulmonary artery the right ventricular pressure increases, the coronary arterial blood supply decreases, and the circulatory reflexes increase the contracting force of the right ventricle, elevation of the right ventricular end-pressure depending on an adequate blood volume. An increase in systemic arterial pressure occurred after even slight constriction of the pulmonary artery, and this is thought to be due to reflexes from pulmonary pressure receptors. *H. E. Holling*

CONGENITAL HEART DISEASE

125. **Simple Pulmonary Stenosis. Pulmonary Valvular Stenosis with a Closed Ventricular Septum**
M. CAMPBELL. *British Heart Journal* [*Brit. Heart J.*] **16**, 273–300, July, 1954. 17 figs., 26 refs.

In the present paper from Guy's Hospital, London, the author first reports that in a series of 1,130 cases of congenital heart disease there were 113 cases of simple pulmonary stenosis, an incidence (10%) which is in close agreement with that reported by Wood (*Brit. med. J.*, 1950, **2**, 639).

He then discusses his findings in 75 proved cases of simple pulmonary stenosis. Of the 75 patients, 44 were without cyanosis at rest, but of these, 15 had peripheral cyanosis in cold weather and 15 on exertion. The remaining 31 patients had central cyanosis at rest, and in all of them it was considered to be due to a right-to-left shunt through some form of auricular septal defect, usually a valvular foramen ovale. The age at onset of cyanosis varied: in some cyanosis had been present from birth; in others it developed after the age of 30. The average age at which it was first noted was 14·4 years. The condition was easily diagnosed, the chief physical signs being a systolic thrill and murmur, most marked at the pulmonary area, with a normal or diminished pulmonary second sound. Nearly all the cyanosed patients showed some degree of clubbing of the fingers, but squatting was unusual, being noted in only 6 of the 31 patients.

The size of the heart varied from normal to very large, but the pulmonary trunk was usually enlarged, this enlargement in some cases involving the left pulmonary artery. Usually, though not invariably, the heart was smaller in the acyanotic than in the cyanotic patients; in general, a large heart was a late sign. Only one patient had a right aortic arch. Marked right ventricular preponderance was noted in the electrocardiogram (ECG) of all the patients with cyanosis, usually with deep T inversion across chest leads to V4 or even to V6. Such an extreme degree of right ventricular preponderance was common though less constant in the acyanotic patients. On the other hand, patients with severe stenosis showed no signs of right ventricular preponderance. In all patients with T inversion to V4 the

right ventricular systolic pressure was over 100 mm. Hg; there were, however, some cases without this pattern in the ECG in which the right ventricular pressure was over 100 mm. Hg. It is considered that the development of inversion of the T wave in Leads V1 to V4 is an indication for operation. In many cases there was a large P wave in Lead II which was associated with a high right atrial pressure; a giant "a" wave in the jugular pulse was observed in such cases. Examination of the heart in 13 cases showed that the stenosis was at the valve cusps, which were fused into a dome-like diaphragm with a small central opening.

The author states that when the stenosis is mild the prognosis is excellent; one personal case is cited, that of a man of 66 in whom the condition had been diagnosed 20 years previously and symptoms had been trivial since. Indications for valvotomy are a right ventricular pressure over 100 mm. Hg, marked right ventricular preponderance in the ECG, a giant "a" wave in the jugular pulse, severe symptoms, and enlargement of the heart. *C. Bruce Perry*

126. **A Study of the Pressure Curves in the Right Ventricle and Pulmonary Artery in Pulmonary Stenosis.** (Étude des courbes de pressions ventriculaire droite et artérielle pulmonaire dans les rétrécissements pulmonaires)
F. BOUCHARD and C. CORNU. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **47**, 417–425, May, 1954. 10 figs.

The authors, writing from the Hôpital Lariboisière, Paris, describe and illustrate the curves obtained by continuous electromanometric recording of pressure during the course of catheterization of the right ventricle and pulmonary artery in 115 cases of pulmonary stenosis with and without other cardiac lesions. They found on drawing the catheter back from the pulmonary artery into the right ventricle that in some cases a point was reached just distal to the valve where the pressure fell during systole below the level recorded elsewhere in the artery or in the ventricle, the curve sometimes registering negative values. In these cases a jet of blood could be palpated at operation, emerging through the stenosed valve during systole.

[The phenomenon described here is surely the Venturi effect, the negative pressure from which is made use of in the ordinary filter pump.] *G. S. Crockett*

127. **The Relation between Tuberculosis and Congenital Heart Disease, with Special Reference to Pulmonary Stenosis.** (Sui rapporti tra tubercolosi e cardiopatie congenite con speciale riguardo alla stenosi della polmonare)
G. FEGIZ and M. MANCUSO. *Archivio di chirurgia del torace* [*Arch. Chir. Torace*] **11**, 401–425, July–Sept., 1954. 17 figs., 17 refs.

It was for long thought that pulmonary tuberculosis and congenital heart disease, especially in its cyanotic forms, were incompatible. This was probably because many seriously affected patients died of the heart disease and mild cases went unrecognized. In fact the association has been reported for almost all types of congenital cardiac lesion, and the incidence is particularly high in pulmonary stenosis.

The authors here present, from the Institute of Surgical Pathology, University of Rome, 3 cases of tuberculosis among 28 patients with pulmonary stenosis, representing an incidence of over 10%, as compared with only one case of tuberculosis among 110 patients with Fallot's tetralogy. The poor pulmonary blood circulation, resulting in an inadequate supply of antibodies and lymph, is thought to predispose to infection, just as the opposite state of affairs which exists in mitral stenosis is thought to protect the lungs. In the 3 cases described pulmonary valvotomy was performed, with subsequent improvement in the tuberculous condition. The first patient had no other treatment, and follow-up examination for over 3 years showed rapid and complete healing; the other 2 patients received streptomycin. Single examples of the association of tuberculosis with tricuspid atresia, the Eisenmenger complex, and transposition of the heart are recorded. No case could be found of associated tuberculosis in patients with atrial septal defect or patent ductus arteriosus. *A. Paton*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

128. **Rehabilitation of the Patient with Coronary Artery Disease**
J. G. KAUFMAN and M. C. BECKER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 9–17, July, 1954. 38 refs.

After myocardial infarction, rest in bed is recommended by the authors for 2 to 8 weeks, depending upon the size of the infarct. After a further month at home about 75% of their patients are able to return to work. Although difficulties may be encountered in the case of unskilled manual labourers who cannot be taught other work, it is felt that a place could be found in industry for most of the remainder, if due allowance is made for possible risk to other employees or to property in the case of a cardiac emergency, and if the liability of the employer to pay compensation could be suitably adjusted. *C. W. C. Bain*

129. **Painless Myocardial Infarction: a Review of the Literature and Analysis of 220 Cases**
M. D. ROSEMAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 1–8, July, 1954. 33 refs.

In 10 out of 220 cases of myocardial infarction proved by necropsy or serial electrocardiography at the Boston City Hospital (Boston University), the patient complained of no pain or discomfort. Only in 5 of the 10 was it possible to obtain a reliable history. Of these, 2 patients had a long history of angina but had no pain at the time of the infarction, and it is considered that in these cases slow and progressive narrowing of the coronary vessels may have resulted in relative anaesthesia of the infarcted area from destruction of the vessels and nerves, so that the final occlusion caused no pain. The other

patients may have been hyposensitive individuals in whom the marked dyspnoea which accompanied the attack overshadowed a moderate amount of pain. From this series and a survey of the literature it is concluded that painless myocardial infarction is rare.

C. W. C. Bain

CHRONIC VALVULAR DISEASE

130. The Apical Systolic Murmur in Mitral Stenosis

P. Mounsey and W. Brigden. *British Heart Journal* [*Brit. Heart J.*] **16**, 255–260, July, 1954. 5 figs., 17 refs.

The significance of the apical systolic murmur as a guide to the presence of regurgitation in cases of dominant mitral stenosis was studied at the London Hospital in 50 patients subjected to mitral valvotomy. Any important degree of mitral incompetence was excluded in all cases by the absence of significant left ventricular enlargement and of expansile left auricular pulsation on radiological examination. The character of the apical systolic murmur, when present, was studied before operation clinically and by phonocardiography, and was related to the state and size of the mitral valve and the degree of regurgitation as estimated by the surgeon's finger.

Where there was no systolic murmur there was no regurgitation in 18 out of 19 cases. Where the murmur was limited to the first half of systole (confirmed by phonocardiogram) regurgitation was absent in 14 and only slight in 8 out of 22 cases. There were 9 patients with a murmur lasting throughout systole ("pan-systolic"): all had some degree of regurgitation which could not with certainty be related to the loudness of the murmur. A pan-systolic murmur was heard in 4 cases during episodes of congestive failure, diminishing on recovery. Softness of the first sound and absence of an opening snap were associated with calcification of the mitral valve and, indirectly, with regurgitation, for this was commoner where there was calcification.

J. A. Cosh

131. Mechanical Principles in the Surgery of Aortic and Mitral Incompetence

R. C. Brock. *British Heart Journal* [*Brit. Heart J.*] **16**, 317–323, July, 1954. 6 figs., 3 refs.

In a short paper the author describes some of the difficulties encountered in the various operations that have been devised to counteract aortic and mitral valvular incompetence. While plastic prostheses have been used to correct mitral incompetence and appear to be tolerated for a short time, the long-term result is not likely to be satisfactory, to judge from the fate of foreign bodies elsewhere. The use of the patient's own tissues, a flap of pericardium being the most popular, is biologically more reasonable, but again there are objections. Firstly, the thin, mobile flap shrinks and becomes fibrotic, thus losing much of its value. Secondly, there is some difficulty in placing such a flap in a satisfactory position to correct mitral incompetence: ideally it should lie across the long axis of the valve opening, but this is impossible as it would pass right across the outflow tract of the right ventricle. Lengthening of the posterior cusp by placing a flap below it is theoretically reasonable, but the risk of impaction of the flap in the orifice is considerable when it is exposed to the axial stream of blood during regurgitation. But whatever means may be found to replace a defective valve, the important factor in many cases of incompetence is dilatation of the atrio-ventricular ring. Functional incompetence of the tricuspid valve secondary to right-sided failure and mitral stenosis is an example, its temporary nature being indicated by the fact that it disappears with medical treatment or after surgical relief of the mitral stenosis. This factor also undoubtedly plays some part in organic insufficiency, and attention should therefore be given towards reducing the size of the ring in any operation for the correction of mitral incompetence.

In aortic incompetence the use of a pericardial flap as an accessory valve to control regurgitation has been investigated experimentally, but without permanent success. Prolapse of the pedicled flap through the valve and fibrosis and increasing rigidity of the flap were the principal causes of failure. This method was tried in 2 cases in man, with fatal results.

The author clearly has little confidence in the procedures introduced so far for the relief of cardiac valvular incompetence.

T. Holmes Sellors

132. Mitral Commissurotomy through the Right Thoracic Approach. Technique and Indications

W. B. Neptune and C. P. Bailey. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **28**, 15–22, July, 1954. 8 figs., 2 refs.

It is sometimes an advantage to be able to approach the mitral valve through the right hemithorax. In this paper from Hahnemann Medical College and the Bailey Thoracic Clinic, Philadelphia, the authors describe such an approach, and suggest its use in cases of mitral stenosis and associated lesions, such as tricuspid stenosis, pulmonary disease in the right lung, and cardiac abnormality.

The approach is carried out as follows. The chest is opened either through the usual posterolateral incision or through an anterior incision in the 4th intercostal space. The pericardium is opened in front of the phrenic nerve and the superior vena cava mobilized by dissection posteriorly in the groove between it and the wall of the left atrium. This exposes the most lateral part of the wall, which is then encircled by a purse-string suture and supported by stay sutures. A stab wound is made into the atrium and the valve examined with the left index finger. If necessary, a valvotome can be introduced in the same manner. It is important to appreciate the altered orientation of the long axis of the valve when palpated from the right side. At the end of the procedure the atrial wall is closed by continuous suture. The authors describe cases in which mitral valvotomy was successfully combined with tricuspid valvotomy, with resection of the right upper lobe for carcinoma, and with repair of an atrial septal defect in a case of Lutembacher's syndrome.

A. M. Macarthur

133. **Pressures in the Left Auricle and Ventricle in Mitral Stenosis before and after Commissurotomy.** (Les pressions de l'oreillette et du ventricle gauches dans la sténose mitrale avant et après commissurotomie)
B. I. LATSCHA, F. D'ALLAINES, and J. LENÈGRE. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **47**, 385–409, May, 1954. 12 figs., 7 refs.

The pressures within the left auricle, left ventricle, and aorta were measured with an electromanometer by direct needle puncture after the pericardium had been opened at operation in 70 patients with mitral stenosis undergoing mitral commissurotomy at the Hôpital Broussais, Paris.

In pure mitral stenosis the left auricular pressure was roughly halved as a result of operation on the valve, the pressure being usually in the region of 30 mm. Hg before operation. The left ventricular systolic pressure was found to be low initially in pure mitral stenosis, the average being 78 mm. Hg, and rose after satisfactory valvotomy to an average of 115 mm. Hg. Except when the mitral stenosis was accompanied by aortic regurgitation, the left ventricular diastolic pressure was normal initially and was unchanged after operation. When mitral incompetence was predominant, the left ventricular pressure was often raised.

The authors made the surprising discovery, by means of simultaneous recording of the pressures within the left ventricle and aorta, that the systolic pressure in severe mitral stenosis may be higher in the aorta than in the left ventricle, this difference being reduced by valvotomy.
G. S. Crockett

134. **Prolonged Treatment with ACTH following Mitral Commissurotomy.** (Trattamento prolungato con ACTH negli operati di commissurotomia mitralica)
G. MAGRI, A. ACTIS-DATO, P. F. ANGELINO, E. JONA, V. LEVI, G. M. MOLINATTI, A. PIZZINI, and M. TEDESCHI. *Cardiologia pratica* [*Cardiol. prat. (Milano)*] **5**, 203–218, April, 1954. 37 refs.

In view of the report by Dogliotti (*Boll. Soc. piemont. Chir.*, 1953, **23**, 3) of the finding of postoperative manifestations of rheumatic relapse in 19 (38%) of 50 patients subjected to mitral valvotomy, these manifestations being present in all of 6 cases with a recent history of rheumatic fever, the present authors have treated 8 patients undergoing this operation at the University Surgical Clinic, Turin, by prolonged administration of ACTH and salicylates with the object of preventing such recrudescence of symptoms. ACTH was given in a dose of 40 mg. daily for 3 days before operation; then on the 7th to 10th postoperative day a weekly cycle of treatment was begun, consisting of 40 mg. of ACTH daily on 3 days and 0·5 g. of amidopyrine as a suppository or 2 g. of aspirin by mouth daily on the other 4 days. After 3 months the dose of ACTH was reduced to 30 mg. per day and this dosage was continued, along with the other drugs, for at least 6 months.

The postoperative course of these patients was slightly better than the average, but in 2 cases symptoms of rheumatic activity occurred. In one case augmentation of the dose of ACTH to 75 mg. daily was required to effect control of the disease. No undesirable side-effects were observed during the careful control of this prolonged treatment. *C. A. Jackson*

135. **Changes in the Radiological Appearance of the Heart and Vessels after Mitral Commissurotomy.** (Le modificazioni della immagine radiologica cardio-vascolare in rapporto all'intervento di commissurotomia della mitrale)
M. GENTILE and M. M. ENRICI. *Annali italiani di chirurgia* [*Ann. ital. Chir.*] **31**, 290–299, 1954. 5 figs., 17 refs.

The authors briefly review the characteristic radiological appearances of the heart in mitral stenosis and describe the immediate and late postoperative modifications observed in 150 patients undergoing mitral commissurotomy at the University Surgical Clinic, Rome.

At first after operation there is an over-all enlargement of the heart shadow mainly affecting the left ventricle. But in cases of pure stenosis relieved by operation, and without postoperative incompetence, regression of this enlargement begins some 20 to 30 days after operation, so that at follow-up examination about 3 years later a nearly complete return to the normal cardiac outline is observed. When, however, incompetence of the valve results in regurgitation a progressive ventricular enlargement persists, this being not merely due to atonia and elongation of the ventricular fibres, as in simple stenosis, but a true ventricular hypertrophy. *C. A. Jackson*

AORTA

136. **New Methods of Surgical Treatment of Degenerative Diseases of the Abdominal Aorta**
O. C. JULIAN, W. J. GROVE, W. S. DYE, H. JAVID, and M. S. SADOVE. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 36–49, July, 1954. 3 figs., 16 refs.

A process of gradual occlusion by deposition of fatty material, fibrosis, and calcification in the region of the aortic bifurcation causes the syndrome described by Leriche (*Presse méd.*, 1940, **48**, 601), of which the main clinical features are intermittent claudication of the lower extremities, sexual impotence, and the absence of pulsation in the femoral arteries. An adequate collateral circulation usually develops, but may be obstructed by proximal extension of the thrombosis, leading to eventual vascular nutritional changes in the limbs. Resection of the aortic bifurcation and its replacement by a homologous graft was first accomplished successfully in 1951 by Oudot (*Presse méd.*, 1951, **59**, 234; *Abstracts of World Surgery*, 1951, **10**, 119). The method has the theoretical advantage over less radical procedures of combining the restoration of normal circulation with prevention of further spread of the obliterative change.

The present authors report the results of this procedure in 14 cases so treated at St. Luke's Hospital (University of Illinois), Chicago; 5 of these cases have been previously reported (*Ann. Surg.*, 1953, **138**, 387; *Abstracts of World Medicine*, 1954, **15**, 316). In 7 of the cases the operation was for Leriche's syndrome and in the remain-

ing 7 for aneurysm of the abdominal aorta. The average age of the patients with Leriche's syndrome was 48, and of those with aneurysm 58. Aortography was not carried out in all cases, as although it was found useful in the selection for operation of cases of Leriche's syndrome it was of little value in the investigation of aortic aneurysm. The authors' surgical technique, which is described and illustrated, is as follows. Grafts are removed aseptically from young adult cadavers and stored at −78° C. Through a left paramedian approach the peritoneum is opened, the aorta and iliac arteries mobilized, the inferior mesenteric artery ligated, and the aortic bifurcation resected. The proximal end of the graft is then anastomosed to the aorta and one distal extremity to one of the common iliac arteries, a continuous everting mattress suture of 5/0 silk, followed by a second layer of continuous suture, being used. The clamps are then removed to flush out clots and replaced on the remaining iliac artery for the final anastomosis. Anticoagulants are not used as a routine. The results are described as "good" or "excellent" in 12 cases; there was no improvement in one case, and one patient died postoperatively. During a follow-up period ranging from one to 24 months no case of delayed stenosis or thrombosis has occurred. *M. A. Birnstingl*

HYPERTENSION

137. **Sympatho-adrenal Surgery in the Malignant Phase of Essential Hypertension**
S. T. R. Revell, F. J. Borges, G. H. Yeager, J. G. Arnold, and R. I. Ahlquist. *Annals of Internal Medicine* [*Ann. intern. Med.*] **41**, 50–69, July, 1954. 8 refs.

This discussion of the value of surgery in the malignant phase of essential hypertension, presented from the University of Maryland School of Medicine, Baltimore, is based on the treatment of 11 such cases by sympathectomy or adrenalectomy, or both, and on observations on 6 other patients who died before treatment could be undertaken. The case histories of all these patients are presented in some detail. Clinical criteria for selection of patients were sought which would enable valid comparisons to be made between different methods of treatment. The criteria adopted were a rapidly progressive hypertensive state, the absence of any demonstrable aetiology, and the presence of papilloedema with haemorrhagic exudates. In 11 of 12 such patients the renal tissue showed necrotizing arteriolitis, and this is considered to show that the patients reported formed (with one exception) a homogeneous group.

Adrenalectomy, partial or total, was carried out on 5 of the patients, all of whom, however, died soon after operation. Thoraco-lumbar sympathectomy in addition to total adrenalectomy was performed on 5 others; only one patient in this group, in whom an empyema ensued, died postoperatively, the remainder having survived for a number of months. One further patient died after the first stage of the double operation. In one of the survivors the impairment of renal function which was present before operation has shown considerable improvement, and it is hoped that later a renal biopsy will show whether necrotizing arteriolitis has been reversed. The authors believe that difficulties with replacement therapy contributed to at least one of the deaths. They conclude that combined adrenalectomy and sympathectomy in this condition is worthy of further trial.

[From the information given, it would appear that renal function was more depressed in patients treated by adrenalectomy alone than in those in whom sympathectomy was also performed, thus favouring the prognosis of the latter group.] *C. J. Longland*

PORTAL CIRCULATION

138. **An Oximetric Study of the Portal Blood.** (Étude oxymétrique du sang porte)
A. Lemaire, E. Housset, P. Casassus, and P. Sée. *Presse médicale* [*Presse méd.*] **62**, 945–946, June 19, 1954. 8 refs.

The authors, working at the Hôpital Saint-Antoine, Paris, have investigated the oxygen saturation of the blood in the portal vein of a number of patients with cirrhosis and compared the findings with those in a control group undergoing partial gastrectomy.

In the latter a sample of portal venous blood was taken at operation and compared with venous blood taken from the arm. In all cases the haemoglobin values, erythrocyte counts, and haematocrit readings were identical, but the oxygen saturation of the portal blood was of the order of 60% whereas the mean value for the systemic blood sample was 42%. From 3 patients with hepatic cirrhosis accompanied by portal hypertension portal blood was obtained in the fasting state from a patent umbilical vein. In each case the oxygen saturation of the portal blood was significantly raised above the mean normal value and above that of the patients' systemic blood taken from the shoulder. In one case in which it was possible to repeat the observations over a period of 4 months the oxygen saturation of the portal blood rose steadily from 65 to 87%. In all these cases there was no change in other blood values, such as haemoglobin level and number of erythrocytes, in the two types of blood. In a further group of 5 cirrhotic patients with no associated vascular malformation the oxygen saturation was again raised in the portal blood, the values ranging from 63 to 76%.

In discussing the possible mechanisms concerned in this consistent increase in the oxygen saturation of the portal blood in patients with hepatic cirrhosis the authors are disinclined to believe that there is an arterio-venous shunt through the liver, as has been postulated by some workers, because on catheterization of the portal vein radicle in one of their cases there was no increase in pressure during systole. They suggest, however, that there may be such a shunt through the spleen, as in this same case analysis of a sample of blood obtained from the splenic vein at operation showed the oxygen saturation to be 92%, a figure very close to that of arterial blood (94%). They conclude that there is no evidence that stasis plays a part in portal hypertension.

T. D. Kellock

Haematology

139. **A Comparison of the T1824 Blood Volume at Sea-level and an Altitude of 5,740 Feet in Normal South African European Males**
B. C. ELLIS. *South African Journal of Medical Sciences* [*S. Afr. J. med. Sci.*] **19**, 11–14, June, 1954. 13 refs.

In an investigation carried out at the University of the Witwatersrand, Johannesburg, the plasma volume was measured by means of azovan (Evans) blue and the erythrocyte volume estimated by means of the haematocrit in 20 healthy men who had been living at sea level in Cape Town, and the values observed compared with those obtained by the same techniques from 20 comparable subjects living in Johannesburg at an altitude of 5,740 feet (1,750 m.). In the former group the mean plasma volume was 43.5 ml. per kg. body weight, the mean erythrocyte volume was 36.6 ml. per kg., and the total blood volume was 80·1 ml. per kg. The mean haematocrit value, uncorrected for trapped plasma, was 47·5%. These results are very similar to those obtained by other workers with the same technique on subjects at sea level. In the latter group the mean plasma volume was 39·3 ml. per kg., the erythrocyte volume 35·8 ml. per kg., and the total blood volume 75·1 ml. per kg. The plasma volume and total blood volume were thus significantly lower than in the group at sea level, but the erythrocyte volume was unchanged. The uncorrected haematocrit value in the latter group was raised to 49·7% by this reduction in plasma volume. It is suggested that the well-known phenomenon of augmentation of erythrocyte volume by altitude occurs only in residents at altitudes over 5,740 feet.

W. A. Briscoe

140. **Lymphosarcoma: an Analysis of Frequency Distribution and Mortality at the University of California Hospital, 1913–1948**
M. B. SHIMKIN, K. C. OPPERMANN, B. V. A. LOWBEER, and S. R. METTIER. *Annals of Internal Medicine* [*Ann. intern. Med.*] **40**, 1095–1107, June, 1954. 3 figs., 16 refs.

The case records of 215 patients with lymphosarcoma seen at the University of California Hospital, San Francisco, between 1913 and 1948 are here analysed. In 95 cases the primary manifestation was peripheral lymphadenopathy; in 52 there were abdominal or thoracic masses, with or without peripheral lymphadenopathy; and in 44 the disease was limited to some special organ such as the stomach, intestines, tonsil, bone, or skin. In the remaining 24 cases the diagnosis of giant follicular lymphoma was made. There were 131 male patients and 84 female. The mean age was 48·2 years, the peak frequency being during the 6th decade. The mean duration of illness in months in the group with peripheral lymphadenopathy was 34, in the visceral group 17, in the group with involvement of some special organ 37, and in cases in the giant follicular lymphoma group 53. The 5-year survival rate for the whole series was 24%, varying from 2% in cases with visceral involvement to 46% in cases of giant follicular lymphoma. Ten patients remained free from evidence of disease for periods ranging from 5 to 21 years after treatment by surgery or irradiation. The survival of patients with peripheral lymphadenopathy who were less than 45 years old was significantly better than that of older patients.

L. J. Davis

141. **Leukemia in Atomic Bomb Survivors. II. Observations on Early Phases of Leukemia**
W. C. MOLONEY and R. D. LANGE. *Blood* [*Blood*] **9**, 663–685, July, 1954. 6 figs., 21 refs.

The authors, working in the laboratories of the Atomic Bomb Casualty Commission, Hiroshima, found 10 cases of leukaemia among 3,480 survivors of the atom-bomb explosion. Their findings indicate that the dose of irradiation causing leukaemia is high, probably in excess of 200 r. Gamma radiation is considered to be the chief agent, but radioactivity induced in phosphorus by neutron effect may also be a cause.

In 7 of the 10 cases there was acute or subacute leukaemia and in 3 chronic myeloid leukaemia. In the chronic form abnormal cells were found in the peripheral blood over 18 months before the clinical onset of the disease. The latent period—that is, the interval elapsing between irradiation and the development of clinical symptoms—was found to vary from 2 to 8 years in chronic myeloid leukaemia. The haematological features in the preclinical stage were leucocytosis with immature cells of the granular series and basophilia. Biochemical studies on the leucocytes in a few cases revealed very low alkaline-phosphatase values. In acute leukaemia, however, it seemed that there was only a short or undetectable preleukaemic phase. The paper concludes with some speculation on the nature of the disorder.

E. G. Rees

142. **The Prognosis for Survival in Chronic Granulocytic and Lymphocytic Leukemia**
H. TIVEY. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **72**, 68–93, July, 1954. 10 figs., bibliography.

Conventional methods of statistical analysis are not satisfactory for evaluating the effect of treatment in certain chronic diseases, such as the chronic leukaemias, because of the markedly skew distribution of survival times. However, an approximately normal distribution curve, similar to the normal probability curve, can be obtained by plotting the logarithms of the survival times. In this way, it is possible for each set of data, to calculate the logarithmic mean, its standard error, and the standard deviation of the series, which can be used for comparing different sets of data. These parameters can be cal-

culated only when the time of survival from the onset of symptoms to death is given for each patient; when some patients in a series are still living, the ultimate results may be estimated by Lea's method (*Cancer Res.*, 1945, **5**, 633) which is based on the " maximum likelihood " method of Fisher.

With these techniques, series of cases of chronic leukaemia reported in the literature between 1925 and 1951 have been reviewed and survival times determined, series of less than 10 cases being excluded. In all, 2,629 cases were reviewed, in 1,978 of which the duration from onset to death was given. For 1,090 patients with granulocytic leukaemia and 685 with lymphatic leukaemia the 50% survival times (the antilogarithm of the log. mean) were, respectively, 2·70 and 2·77 years. The distributions overlapped almost completely and therefore no difference in prognosis between the two types of leukaemia could be demonstrated. For the total of 1,978 cases (including 203 in which the distinction between lymphocytic and granulocytic leukaemia was not made) derived from 32 published series the 50% survival time was 2·65 years (95% confidence limits 2·59 to 2·69 years). Analysis showed that this figure was not dictated by one series of patients.

There was poor correlation between the log. means and approximate mid-date of each study, suggesting that there has been no marked over-all improvement in the treatment of leukaemia over this period. However, for those patients treated with radioactive phosphorus (^{32}P) the 50% survival times for lymphocytic, granulocytic, and both types of leukaemia were 3·20, 3·08, and 3·29 years respectively, these values differing significantly from the over-all values. Since not all these patients were treated with ^{32}P alone, however, this improvement can be attributed only to the total care given these patients, of which ^{32}P was a part. In 651 cases it was possible to estimate the survival time after the beginning of therapy. The 50% point was 1·56 years.

The author has applied this statistical technique to a series of 58 patients treated by Osgood's method with ^{32}P or total-body *x*-ray therapy (*Arch. intern. Med.*, 1951, **87**, 329; *Abstracts of World Medicine*, 1951, **10**, 177). The 50% survival time after onset of symptoms was 4·8 years, and that after treatment 2·5 years. These times are significantly greater than those calculated from the results reported in the literature for any other form of treatment. *M. Lubran*

143. **Leukemic Xanthomatosis**

P. Freud, A. Plachta, F. D. Speer, and A. L. Luhby. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **88**, 43–61, July, 1954. 15 figs., 48 refs.

A case of " leukaemic xanthomatosis ", which, the authors state, is a hitherto unknown disease, is reported in this paper from New York Medical College and Flower and Fifth Avenue Hospitals. Xanthomatous skin lesions were first seen when the patient, a boy of Puerto-Rican extraction, was 2 years old, and the condition progressed through a leukaemic phase with gross hepatosplenomegaly until the patient died at the age of 5 years 3 months. Detailed clinical and necropsy findings are given. The occurrence in the reticuloendothelial organs of large numbers of cholesterol-laden primitive foam cells of histiocytic variety enmeshed in abundant argyrophilic reticulum and of numerous extramedullary foci of haematopoiesis was of particular note. The importance of the common origin of the cholesterol cells and blood cells from mesenchymal embryonic elements is emphasized; this is regarded as establishing a link between the aleukaemic forms of systemic reticuloendotheliosis and the leukaemias.

The question whether leukaemic xanthomatosis is a neoplastic or a hyperplastic process is discussed, but no conclusion is drawn. The possibility that a virus infection is the cause is also discussed, suggestive factors being the presence of inclusion-body cells in the parenchyma of affected organs and previous reports of amelioration of the disease by antibiotics. *Mary D. Smith*

144. **The Role of Tissue Antigens in Haemolytic Disease of the Newborn**

I. Brading and R. J. Walsh. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **32**, 213–220, April [received Aug.], 1954. 14 refs.

In experiments carried out at the Red Cross Blood Transfusion Service, Sydney, in an attempt to elucidate the role of tissue antigens in the production of haemolytic disease of the newborn, tissue emulsions from the liver, kidney, spleen, heart, and brain prepared in a Waring blender were freed from erythrocyte stromata by repeated centrifugation through distilled water. Various methods of elution of antibody from the tissues were employed and these are described in detail. The eluates were tested by the indirect Coombs test.

It was shown that homogenized, washed emulsions of tissues from normal Rh-positive infants absorbed anti-D antibody from serum. Anti-D was also eluted from similar preparations of the organs of 12 babies dying of haemolytic disease, while anti-C antibody was eluted from the washed tissue homogenates of a baby from a mother with anti-C antibodies in her serum. The results confirm the observations of Boorman and Dodd (*J. Path. Bact.*, 1943, **55**, 329) who first showed that tissue cells contain Rh antigens. The findings also prove that Rh antibodies from a mother become attached to the tissue cells of her baby with haemolytic disease. The hypothesis is put forward that Rh antibodies can damage tissues as a result of uniting with their corresponding antigens in the tissue cells.

The authors conclude that exchange transfusion is the treatment of choice for babies with haemolytic disease, since by this means antibodies are washed from the circulation, thus allowing antibodies to be eluted from the tissues. However, as they point out, in 3 of the cases investigated exchange transfusion had in fact been given, but in spite of this antibody could still be eluted from homogenized tissues from these patients. They suggest that a more thorough elution of antibody might be obtained by exchange transfusion using Rh-positive blood, although they admit that there are objections to this method. *John Murray*

Otorhinolaryngology

145. **Some Electro-mechanical Properties of the Organ of Corti**
G. VON BÉKÉSY. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol.* (*St. Louis*)] **63**, 448–468, June, 1954. 16 figs., 2 refs.

The author, writing from Harvard University, discusses two ways of studying function in the organ of Corti. The first is by direct observation with the microscope, the second by the use of microphonics. The optical method, even at a magnification of 300, has the disadvantage of showing the vibrations only when they reach their greatest size; an advantage of this method, however, is that it can be used for observing small objects such as cells; recently killed animals may be used, as the cochlea still vibrates for some time after death although the electrical potential disappears when the animal dies.

With the microscope, Hensen's cells were seen to vibrate under a sound stimulus of 200 c.p.s. and they did so in three different ways, depending on their situation in the cochlea, but it is not yet known which of the three ways excites the auditory nerve. The basilar membrane also vibrates with the sound, but this vibration is not thought to have much importance in hearing. The high sensitivity of the ear is one of the most intriguing problems of the physiology of hearing. The author believes it may be due to the shearing mechanism between the tectorial membrane and the organ of Corti.

By electrical methods of study the author has shown the presence of comparatively large differences of potential in the cochlea, although he has not yet succeeded in finding which structure is responsible for them. He suggests that the large difference in potential may react to the effect of sound as a valve amplifier reacts to the current which enters it.

[This clearly written and well-illustrated article cannot be adequately abstracted and should be read in its original form.] *William McKenzie*

146. **The Excitation of Nerve Impulses in the Cochlea**
H. DAVIS. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol.* (*St. Louis*)] **63**, 469–480, June, 1954. 7 figs., 12 refs.

It is well known that a low frequency will mask a high frequency, but a high frequency will not mask a low one. Tasaki showed that a nerve fibre from the basal turn of the cochlea was capable of responding to a tone of 500 c.p.s., besides its accepted sensitivity to high frequencies. He also showed that the response was fairly even to frequencies as high as 8,000 c.p.s. but above this frequency the response was very slight. The general response was, on the whole, similar to the reaction of the auditory nerve itself. Békésy has shown that the endolymph in the scala media is electrically positive in relation to the perilymph, and has also demonstrated a negative potential in the cells of Reissner's membrane, similar to the negative potential inside the axon of a nerve fibre. The negative potential is sensitive to lack of oxygen and in conditions of anoxia falls nearly to the same degree as the cochlear microphonic.

The present author has now shown by experiment that the electrical potential of the scala media is increased by hydrostatic pressure in the scala media or scala vestibuli. This change in pressure is probably caused by displacement of the basilar membrane. The cochlear microphonic is probably closely related to this potential, for if the potential is made to increase, the cochlear microphonic increases also. Again, if the perilymph in the scala tympani is replaced by Ringer's solution, the cochlear microphonic and nerve impulse are abolished, but not the negative potential, so that the two can be separated in these circumstances. It seems certain that the anatomical source of the cochlear microphonic is the hair-bearing end of the hair cells. Whereas the scala media is filled with endolymph, the tunnel of Corti is filled with perilymph, and the barrier between is the reticular membrane, which is impermeable to ions. The cochlear microphonic is probably the immediate stimulus of the nerve impulse. *William McKenzie*

147. **Positional Nystagmus**
T. CAWTHORNE. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol.* (*St. Louis*)] **63**, 481–490, June, 1954. 8 refs.

Positional nystagmus is the term used for nystagmus which is produced by sudden extension of the head and body of a subject who is first examined in the sitting position. The nystagmus is usually accompanied by vertigo and is thought to be due to a disorder of the labyrinth. The author reports that in two-thirds of such cases seen at the National Hospital for Nervous Diseases, Queen Square, London, there was no other sign of labyrinthine disease. The condition is benign and the pathology is still obscure.

Positional nystagmus occurs sometimes after head injury, or it may be associated with a focus of infection, such as an infected tooth or antrum. When due to a disordered labyrinth it is usually seen when the head is extended and turned so that the affected ear is lowermost. The reaction is limited, and may not appear when the head is extended a second time if the interval between the two examinations is too short. The complaint is commoner in women than it is in men, probably because women have to stoop more when doing housework. Remissions are typical, and patients may be free from symptoms for several weeks at a time. In contrast, positional nystagmus of central origin appears when the head is extended and can always be elicited no matter how quickly the test is repeated. *William McKenzie*

Urogenital System

148. **Epidemic Nephropathy.** (Nephropathia epidemica)
B. TUNGLAND. *Nordisk Medicin* [*Nord. Med.*] **51**, 635–639, May 6, 1954. 1 fig., 16 refs.

The author describes 28 cases of epidemic nephropathy seen at Hedmark Hospital, Elverum, Norway, 20 of which occurred during the winter of 1948–9. Only 2 of the patients were women, the majority of the remainder being foresters between 20 and 40 years of age. Backache, headache, and abdominal pain were the commonest symptoms, and the objective findings were proteinuria (in every case but one), azotaemia (23 cases), and a raised erythrocyte sedimentation rate (21 cases). The specific gravity of the urine was low, and polyuria developed in the second week of the illness. Only very small numbers of cells and casts were found in the urine at any time. The commonest erroneous diagnosis was one of acute nephritis, but in the absence of hypertension, haematuria, and a concentrated urine this mistake should not have been made.

The condition seems to be an acute infectious disease attacking persons living in primitive hygienic conditions. Evidence points to the causative agent being transmitted by mice. The incubation period appears to be between 2 and 6 weeks. The prognosis is good, 10 of the patients showing no sign of renal disease when seen 5 years after the attack. *B. Nordin*

149. **Biopsy of Kidney in Prone Position**
R. M. KARK and R. C. MUEHRCKE. *Lancet* [*Lancet*] **1**, 1047–1049, May 22, 1954. 3 refs.

The authors have found unsatisfactory the technique of renal biopsy described by Iversen and Brun (*Amer. J. Med.*, 1951, **11**, 324; *Abstracts of World Medicine*, 1952, **11**, 24) in which the patient stands upright. In this paper from the University of Illinois College of Medicine, Chicago, they describe their own technique, which has proved highly satisfactory. Briefly, the patient lies in the prone position with a sand-bag beneath the lower abdomen. The kidney, preferably the right, is located with a fine exploring needle through which a local analgesic is injected. Biopsy is then carried out with a modified Vim–Silverman needle, now available commercially. The procedure must be carried out in hospital and only after investigations have been made to exclude haemorrhagic diathesis, perinephric abscess, aneurysm of the renal artery, tumours and large cysts of the kidney, and the possibility of a solitary kidney.

Of 50 biopsies made on 47 patients, 48 were technically successful. The 2 failures occurred in a patient with very small, mobile kidneys and in another with a large hydronephrosis. In only one of the 48 successful biopsies was the tissue obtained insufficient for diagnostic purposes; in 25 cases biopsy examination changed the clinical diagnosis and in the other 22 cases it confirmed the clinical diagnosis. Renal biopsy was always followed by microscopic haematuria, and in 4 patients by gross haematuria, which in one case was such as to necessitate blood transfusion. Only 5 of the patients had mild pain during the procedure and 6 others complained of some pain after the effects of the local analgesic had worn off.

[Those interested in the possibilities of renal biopsy should consult the original article.] *K. G. Lowe*

150. **A Study of 37 Children with Lipoid Nephrosis Followed up for 2 to 16 Years.** (Sur 37 néphroses lipoïdiques de l'enfant, suivies de 2 à 16 années)
J. MARIE, P. SERINGE, and C. POLONOVSKI. *Annales de médecine* [*Ann. Méd.*] **55**, 252–302, 1954. Bibliography.

Of 37 children with lipoid nephrosis who were under the care of the authors at the Hôpital des Enfants Malades, Paris, between 1934 and 1952 and were followed up for periods varying from 2 to 16 years, 12 made a complete recovery (confirmed by repeated examinations), and 10 have some permanent functional damage, of whom 2 have persisting albuminuria, while 2 have developed chronic nephritis and one hypertension. Ten of the children died after an illness lasting from one month to 6 years; in 4 cases death was due to an intercurrent infection, in 5 the cause was unknown, and one child died suddenly after an intravenous injection of a mercurial diuretic. The remaining 5 children were followed up for less than 3 years and the final stage of the illness has not yet been reached.

Not infrequently, though more often during the earlier phase of the disease, the patients suffered from microscopic haematuria or even gross haematuria, with or without a temporary rise in the systolic blood pressure, but this phenomenon was thought to have no bearing on the course of the illness, since it was present in one-third of the children who recovered completely. In 31 cases therapeutic measures included as a matter of routine a high-protein diet combined with thyroid extract. During the war a high-protein diet was not always possible, yet it was the only treatment given in 7 cases out of the 12 showing complete recovery. Other measures, such as the administration of diuretics, exchange blood transfusions, concentrated plasma or simple blood transfusions, gave indifferent results. During their stay in hospital 14 children contracted measles, some accidentally and some by medical intention; the majority of these children, after an initial exacerbation of their nephrotic signs, seemed to benefit from it, as shown by rapid reduction of the oedema and improvement in the blood chemistry. The authors stress the lowered resistance of the nephrotic child to intercurrent bacterial infections, and point out that in the pre-chemotherapeutic era one-third of all deaths of such patients were due to these infections. [Unfortunately the authors offer no observations on over-all results since that period, but the paper contains many valuable remarks on the pathology of lipoid nephrosis.] *L. H. Worth*

Endocrinology

PITUITARY GLAND

151. **Growth Hormone and Carbohydrate Metabolism**
R. C. DE BODO and M. W. SINKOFF. *Diabetes* [*Diabetes*] 3, 87–93, March–April, 1954. 7 figs., 22 refs.

The authors, writing from New York University College of Medicine, report the effects of growth hormone on the carbohydrate metabolism of normal, adrenalectomized, adrenalectomized–gonadectomized, hypophysectomized, and adrenalectomized–hypophysectomized dogs. The dosage of growth hormone varied from 0·02 to 2·0 mg. per kg. body weight per day given intramuscularly. All the experiments were performed during the post-absorptive state, that is, 17 to 18 hours after the last intake of food. Carbohydrate metabolism was studied by means of insulin sensitivity, which was determined as the response to 0·025 unit of insulin per kg. body weight, given intravenously, and glucose tolerance as the response to the intravenous infusion of 0·075 g. of glucose per kg. body weight per minute for 10 minutes. The adrenalectomized dogs were maintained on daily minimal doses of deoxycortone acetate (DCA).

It was found that the adrenalectomized dog maintained on DCA showed a similar insulin sensitivity to that of the normal dog, and this held true even after DCA had been withdrawn for periods of 8 to 14 days and signs of adrenal insufficiency had supervened. In contrast to this, adrenalectomized–hypophysectomized dogs, also maintained on DCA, showed a steep fall in blood sugar level after administration of insulin, followed in many cases by hypoglycaemic convulsions. In response to intravenous glucose the adrenalectomized dog manifested a secondary hypoglycaemia, which was even more severe in the adrenalectomized–hypophysectomized animal. The adrenalectomized–gonadectomized dog showed a similar response to insulin and glucose as did the adrenalectomized–non-gonadectomized animal.

Hypophysectomized dogs treated with cortisone or hydrocortisone in a dosage of 0·83 to 1·4 mg. per kg. body weight per day still showed increased insulin sensitivity and secondary hypoglycaemia after glucose, and no significant effect was produced by thyroxine in dosage sufficient to produce clinical hyperthyroidism. But after 3 to 4 days of administration of growth hormone (1 mg. per kg. per day) insulin hypersensitivity was abolished in the hypophysectomized dog and a diabetic type of glucose tolerance with resistance to large doses of insulin developed in every case. Insulin hypersensitivity was also abolished in adrenalectomized–hypophysectomized dogs, thus ruling out the possible influence of ACTH contamination.

Even when growth hormone was administered alone in the smallest effective dose (0·02 mg. per kg. per day), a diabetic tendency eventually appeared in about 50% of the dogs. This could be prevented in hypophysectomized dogs—even in those receiving prolonged administration of large doses of growth hormone (1·0 to 1·5 mg. per kg. per day)—by the concurrent administration of cortisone.

From these experiments the authors conclude that, under physiological conditions, growth hormone acts in concert with the adrenocortical steroids in the endocrine control of normal carbohydrate metabolism.

D. G. Adamson

152. **Metabolic Studies on the Effects of Crystalline Growth Hormone (Somatotropin) in Man**
E. SHORR, A. C. CARTER, B. J. KENNEDY, and R. W. SMITH. *Diabetes* [*Diabetes*] 3, 94–98, March–April, 1954.

The authors report, from Cornell University Medical College and New York Hospital, the metabolic effects of crystalline growth hormone (" somatotropin ") administered to 2 young female patients (aged 14 and 17 years) for 11 and 3 weeks respectively. Both patients were of abnormally short stature, and the elder suffered from thyroid insufficiency and other signs of endocrine imbalance. They were maintained on diets constant in respect of caloric value and carbohydrate, fat, protein, calcium, and phosphorus content, and after a control period were given somatotropin in doses averaging 120 mg. daily (total doses 9·38 and 3·45 g. respectively). In both cases there was enhanced storage of nitrogen, calcium, and phosphorus, with the development of impaired glucose tolerance and increased insulin resistance. These changes were reversed on stopping treatment with the growth hormone.

When administered to 3 boys aged 15, 15, and 13, also of short stature but without associated endocrine abnormality, various preparations of growth hormone, some of which had produced anabolic effects in the females, caused no metabolic changes.

D. G. Adamson

153. **Coma and Allied Disturbances of Consciousness in Hypopituitarism**
J. E. CAUGHEY and O. GARROD. *British Medical Journal* [*Brit. med. J.*] 2, 554–560, Sept. 4, 1954. 2 figs., 23 refs.

Impairment of consciousness varying from hypersomnia to profound coma readily occurs in hypopituitarism and was formerly usually attributed to hypoglycaemia. In this paper the authors discuss the various factors which appear to precipitate loss of consciousness, the mechanism of such loss, and its treatment, with special reference to 17 of their own cases, 10 of which have been reported elsewhere (Caughey, *Aust. Ann. Med.*, 1954, 3, 26). Prolonged coma followed operation upon the pituitary gland in 4 of the cases and a fatal coma followed haemorrhage into a cystic tumour in one other. In such cases coma may be determined by local mechanical

factors rather than by endocrine or metabolic upsets—with which this paper is mainly concerned.

Infections were found to be an important factor in initiating disturbances of consciousness. In 8 cases acute infections such as coryza, influenza, or gastro-enteritis precipitated at first drowsiness and later coma. Coma was caused by hypoglycaemia occurring spontaneously in one case and by the performance of an insulin tolerance test in another; but hypoglycaemia does not, in the authors' experience, usually accompany disturbances of consciousness. In 3 of their cases the patient went into prolonged coma after the administration of drugs or of an anaesthetic, while in 2 further cases coma was associated with sodium loss; this may occur during the early stages of cortisone therapy, when salt is lost during the water diuresis that follows its administration in hypoadrenalism. Water intoxication readily occurs in hypopituitarism, and appeared to provoke mental symptoms in one of the authors' cases. Postural fainting occurred in 6 cases.

The authors have been unable to find any measurable biochemical disturbance common to all cases of hypopituitary coma, but largely because the coma can be prevented by adequate corticosteroid therapy—which provides the most satisfactory treatment for established coma—they conclude that adrenal failure is probably the major factor in the genesis of this disorder. In discussing the treatment of hypopituitary coma they emphasize the need to treat also any infection present, with antibiotics if appropriate, and recommend the routine administration of glucose and saline intravenously to counteract any possible hypoglycaemia. Hydrocortisone or microcrystalline cortisone acetate should be given intravenously at first and subsequently by nasal tube until consciousness is recovered. If the body temperature is very low the patient may be immersed in a warm bath.

Nigel Compston

THYROID GLAND

154. ***In vitro* Conversion of Thyroxin to Triiodothyronine by Kidney Slices**

E. C. ALBRIGHT, F. C. LARSON, and R. H. TUST. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 137–140, May, 1954. 3 figs., 13 refs.

In a study of the conversion of thyroxine to triiodothyronine by kidney slices *in vitro*, carried out at the University of Wisconsin Medical School, male rats of 150 to 200 g. body weight were killed by decapitation, the kidneys removed aseptically, and thin slices representing one-half of a kidney were placed in Warburg flasks containing 3 ml. of Krebs–Ringer solution supplemented with 0·03 mg. glucose, to which was added 0·01 μg. of chromatographically pure thyroxine labelled with radioactive iodine (^{131}I). The flasks were then incubated at 37° C. for various periods up to 12 hours. At the end of this period the slices were removed, dried on blotting paper, weighed, washed to remove excess radioactive thyroxine, and then homogenized in 2 ml. of distilled water, the *p*H being adjusted to 3·0 by the addition of 0·1 N hydrochloric acid. The radioactivity of the entire homogenate was determined by means of a well-type scintillation counter, initially and after each extraction procedure, the homogenates being extracted five times with 6-ml. portions of butanol and the butanol extracts pooled and evaporated to dryness at room temperature. This removed 95% of the radioactivity. The residue was dissolved in 0·1 ml. of butanol containing 50 μg. of carrier L-triiodothyronine and subjected to single-dimension chromatography.

Significant radioactivity appeared at the triiodothyronine spot after 3 hours' incubation, and increasing amounts after 6, 9, and 12 hours. The conversion was reduced in the presence of excess potassium iodide or 0·01 M potassium cyanide, or by boiling. A radioactive spot appeared behind the developer front; this was not identified, but was shown not to be iodine. These findings are considered to show that the extra-thyroidal conversion of thyroxine to triiodothyronine can occur, at least in the kidney.

Norval Taylor

155. **Some Differences in the Metabolism of Thyroxine and Triiodothyronine in the Rat**

N. F. MACLAGAN and J. H. WILKINSON. *Journal of Physiology* [*J. Physiol. (Lond.)*] **125**, 405–415, Aug. 27, 1954. 2 figs., 22 refs.

156. **The Thyro-hypophysial Syndrome in Thyrotoxicosis.** (Tyreo-hypofysärt syndrom vid tyreotoxikos)

B. A. LAMBERG. *Nordisk Medicin* [*Nord. Med.*] **51**, 874–878, June 24, 1954. 7 figs., bibliography.

The thyro-hypophysial syndrome (oedema of the lids, malignant exophthalmos, facial and temporal oedema, and localized myxoedema) is manifest in slight degree in about 60% of cases of hyperthyroidism. In this review of the treatment of the syndrome and the co-existing thyrotoxicosis the author quotes his experience in 5 cases in support of his contention that the exophthalmos can be controlled by careful adjustment of the dosage of antithyroid drugs combined with irradiation of the pituitary gland where necessary. Repeated estimation of the serum protein-bound iodine content is of value in the management of the case, since deterioration in the condition of the eyes may be expected when this value falls to very low levels. Similarly, a rise in the serum cholesterol level is regarded as a bad sign.

B. Nordin

157. **The Fluorescein Circulation Time in Thyrotoxicosis**

A. GEE. *British Medical Journal* [*Brit. med. J.*] **2**, 446–448, Aug. 21, 1954. 8 refs.

The circulation time in cases of thyrotoxicosis was compared with that in cases of non-toxic goitre and of anxiety state, a modification of the fluorescein technique of MacGregor and Wayne being used. This consists in the measurement of the time-interval between the intravenous injection of fluorescein at one antecubital fossa and the development of fluorescence in weals produced by the intradermal injection of histamine in the opposite antecubital fossa and at the base of each hallux. The fluorescence is observed by means of a Wood's

light in a darkened room and the end-point is "clear and instantaneous"; the difference between the times taken for development of fluorescence in the arm and in the feet is normally constant at between 8 and 13 seconds.

Since anxiety was found to shorten the circulation time, all patients were first told what the procedure entailed and also given 6 grains (0·4 g.) of soluble amylobarbitone one hour before the test. Of 26 patients with a clinical diagnosis of thyrotoxicosis, the circulation time was shortened in 25, whereas it was normal in 14 patients with enlargement of the thyroid but no clinical evidence of thyrotoxicosis and in 19 out of 20 patients with anxiety state or other psychiatric disorders causing dyspnoea, tachycardia, or loss of weight. *A. C. Crooke*

158. **Treatment of Recurrent Hyperthyroidism with Radioactive Iodine**

B. G. ANDERSON. *Metabolism* [*Metabolism*] **3**, 297–302, July, 1954. 10 refs.

The efficacy of radioactive iodine (^{131}I) in the treatment of hyperthyroidism is well established, but the most suitable type of patient and the best method of estimating the optimal dose are still matters for discussion. In this study carried out at New England Center Hospital, Boston, 87 patients (67 women and 20 men, average age 47·7 years) were treated for recurrent hyperthyroidism with ^{131}I, 72 of them having been previously treated unsuccessfully by other methods. They were followed up for 6 months and of the 87 patients, 85 were cured, 56 after a single dose and 22 after 2 doses.

Calculation of the dosage was based on the size of the thyroid gland, the percentage uptake by the gland of a trial dose of ^{131}I, and the effective half-life of such a dose. The only complications seen were transient hypothyroidism in 5 cases and permanent myxoedema in another 5; in the majority of cases the thyroid gland returned to normal size. The ease of obtaining a remission depended upon the size of the gland and the severity of the condition. *F. W. Chattaway*

159. **Antithyroid Drugs plus Roentgen Irradiation in the Treatment of Hyperthyroidism**

J. BÖE and Z. GABRIELSEN. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **14**, 939–947, Aug., 1954. 15 refs.

This paper from the University Clinic, Bergen, describes the treatment of 140 cases of hyperthyroidism with antithyroid drugs combined with *x*-irradiation of the neck. The authors suggest that the hyperplasia induced by antithyroid drugs (despite the reduction in secretory activity) may render the gland more sensitive to irradiation. The patients were treated in the usual manner with methylthiouracil, propylthiouracil, or methimazole, the initial doses being generally 600 mg., 400 mg., and 15 mg. daily and the maintenance doses 100 to 200 mg., 50 to 100 mg., and 5 mg. daily respectively. After clinical improvement became apparent (usually within 4 weeks) the neck was irradiated on 9 consecutive days to a total dose of 1,800 to 2,700 r, drug therapy being continued thereafter for a total period of 3 months to 5 years.

All patients attending the clinic with hyperthyroidism received this treatment, with the exception of a few who had very large goitres or who had pressure symptoms and were therefore treated surgically. Out of 140 patients, 13 failed to complete treatment, 28 were still under treatment at the time of the report, and 17 were referred for surgery or treatment with radioactive iodine for various reasons, while 82 completed the course of combined drug and *x*-ray therapy. Of these 82, 67 were regarded as cured after being followed up for at least 6 months (average 15·9 months), 4 were improved, and 11 were considered to be "probably cured", but had not been followed up for as long as 6 months at the time of the report. Toxic effects attributable to the antithyroid drugs occurred in 32 of the 140 patients; there were 7 cases of agranulocytosis during treatment with methylthiouracil and one case after treatment with methimazole.

From a comparison of their results with those obtained by other workers using antithyroid drugs alone the authors conclude that the addition of *x*-irradiation to antithyroid drug therapy does not appreciably shorten the period of treatment necessary to obtain a permanent remission and offers no definite advantage over treatment with drugs alone, though they suggest that it may possibly increase the number of permanent remissions.

Charles Rolland

160. **A Four-year Study of the Treatment of Hyperthyroidism with Methimazole**

J. CHEVALLEY, T. H. MCGAVACK, S. KENIGSBERG, and S. PEARSON. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **14**, 948–960, Aug., 1954. 35 refs.

In this paper from the Metropolitan Hospital (New York Medical College), New York, the authors report and analyse their experience in the treatment of 184 cases of hyperthyroidism with methimazole since 1949. The first 60 patients started treatment with doses of 5 to 20 mg. daily, but thereafter initial doses of 30 to 40 mg. daily were given, this having to be increased in rare cases to 60 mg. daily to control the thyrotoxicosis. The maintenance dose was 2·5 to 30 mg. (usually 20 mg.) daily. In 77 out of 150 cases in which the necessary information was recorded there was both subjective and objective evidence of improvement within a week of starting treatment, while 113 out of 137 patients became euthyroid within 5 weeks. It was noted that improvement was less rapid in the patients whose treatment began with the smaller doses.

Of the whole series of 184 cases, 51 were not satisfactorily followed up, 37 were given preoperative treatment only, and 41 were still receiving methimazole at the end of the period of study. Of the 55 patients whose treatment was completed, 34 were considered to be cured, having remained free of all evidence of hyperthyroidism for at least 4 months (average 15 months) after the cessation of treatment. Most patients who were treated for less than 6 months relapsed. Decrease in size of the thyroid gland and cure of the hyperthyroidism were more frequently obtained in younger than in older patients.

Toxic reactions occurred in 8 cases (4·3%), taking the form of pruritus and localized rashes in 4 cases (one of these with oedema), granulocytopenia not amounting to agranulocytosis in 3, and urticaria with fever in one. The most severe toxic effects were seen in patients receiving 40 mg. or more daily. Increase in size of the neck was noted in approximately one-eighth of the cases. Small doses of iodine were given daily as soon as the patients became euthyroid and this may have encouraged involution of the thyroid. The authors conclude that methimazole is a rapidly acting, relatively safe, and effective antithyroid compound. *Charles Rolland*

161. **17-Ketosteroid and Pituitary Follicle-stimulating Hormone Excretion in Myxedema, before and during Treatment with Thyroxine**
W. H. BEIERWALTES and R. C. BISHOP. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **14**, 928–938, Aug., 1954. 5 figs., 12 refs.

It has been reported that urinary 17-ketosteroid excretion is decreased in myxoedematous patients and that treatment with thyroid fails to restore it to normal. It has also been reported that post-menopausal myxoedematous women excrete reduced amounts of pituitary follicle-stimulating hormone (F.S.H.), but that its excretion rises during the treatment of such patients with thyroid. The effect on 17-ketosteroid and F.S.H. excretion of treatment with increasing doses of sodium L-thyroxine to the point of thyrotoxicosis was investigated at the University of Michigan Hospital, Ann Arbor, in 20 cases of myxoedema. The patients were 6 pre-menopausal women, 9 post-menopausal women, and 5 men. The initial dose of sodium L-thyroxine was usually 0·05 mg. daily and this was increased over a period of months to as much, in some cases, as 1·0 mg. daily. When signs of thyrotoxicosis appeared the dose was reduced or the treatment was stopped.

In several cases there was a rise in 17-ketosteroid excretion from subnormal to normal, but never to supernormal, levels during treatment with thyroxine, and a decrease in excretion when treatment was stopped. F.S.H. excretion was initially normal in the men and pre-menopausal women, but was low in the post-menopausal women and failed to increase even when the dose of thyroxine was increased to the point of causing hyperthyroidism. In one man and one pre-menopausal woman a rise in F.S.H. excretion occurred during thyroxine therapy.

The authors discuss, but are unable to explain, the mechanism and significance of these changes in 17-ketosteroid and F.S.H. excretion in myxoedematous patients. *Charles Rolland*

162. **Hypothyroidism as an Inborn Error of Metabolism**
J. H. HUTCHISON and E. M. MCGIRR. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **14**, 869–886, Aug., 1954. 5 figs., 35 refs.

This paper from the Royal Hospital for Sick Children and the Royal Infirmary, Glasgow, describes a study of three groups of hypothyroid children. The first group of 8 were all related and belonged to a family in which the marriage of cousins was common. [An interesting family tree is provided.] The second group was of 3 unrelated children with retarded growth and mental development and mild features of myxoedema. The third group consisted of 2 half-sisters who were typical cretins. The clinical features and the age at the time of diagnosis varied considerably within the series. Not one of the patients came from an area of endemic goitre and all responded with some improvement when treated with thyroid.

The uptake of radioactive iodine (^{131}I) by the thyroid gland was abnormally rapid and high in 6 cases, but release of the isotope from the gland was similarly rapid. In 8 out of 10 cases the total plasma radioactivity 48 hours after the administration of ^{131}I was more than 0·7% of the dose per litre, which is the maximum normal level reported in Great Britain. At the same time, in 7 out of 10 cases the serum protein-bound ^{131}I content was more than 0·4% of the dose per litre, which is usually taken to indicate hyperthyroidism.

The authors therefore conclude that much of the protein-bound ^{131}I discharged from the thyroid in these cases was in the form of neither thyroxine nor triiodothyronine. They suggest that familial hypothyroidism may be due to an inborn error of metabolism interfering with the synthesis of the thyroid hormone and that it may be transmitted by a recessive autosomal gene. *Charles Rolland*

163. **Oral L-Thyroxine-sodium in Treatment of Myxoedema.** (L-thyroxin-natrium ved myxødem)
E. LUND. *Nordisk Medicin* [*Nord. Med.*] **51**, 880–881, June 24, 1954. 1 fig., 15 refs.

At Rigshospitalet, Copenhagen, 9 patients with myxoedema were treated with sodium L-thyroxine for 2 to 26 months. Response to treatment was rapid and sustained. The author stresses the advantage of using a pure substance that can be prescribed by weight rather than a preparation for which biological standardization is necessary. *B. Nordin*

ADRENAL GLANDS

164. **Action of Hydrocortisone on Cells in Tissue Culture**
H. GROSSFELD and C. RAGAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **86**, 63–68, May, 1954. 4 figs., 11 refs.

The authors describe experiments carried out at the Presbyterian Hospital and Columbia University, New York, which confirmed that hydrocortisone, when added in a concentration of 200 μg. per ml. to chick-embryo tissue cultures in a medium composed of chicken plasma and amniotic fluid, consistently inhibited the growth of fibroblasts. This effect could be partially antagonized by the addition of embryonic extract. The growth of gastric and intestinal epithelium was not inhibited by hydrocortisone. In heart-tissue cultures the fibroblasts whose growth had been inhibited grew normally when the hydrocortisone was removed. Aqueous soluble deoxycortone produced similar effects to those of hydro-

cortisone. Minimal inhibition of growth was also seen when cholesterol in suspension was added.

Similarities and differences between these findings and those usually seen *in vivo* are indicated and discussed. The cause of the inhibitory action of embryonic extract is not clear. *Norval Taylor*

165. **Cortisone and Calcium Balance (Effect of Calcium, Vitamin-D and Methylandrostenediol).** [In English]
F. FISCHER and B. HASTRUP. *Acta endocrinologica* [*Acta endocr. (Kbh.)*] **16**, 141–148, June, 1954. 1 fig., 20 refs.

At the Rigshospital, Copenhagen, the authors have studied the effect of calcium, vitamin D, and methylandrostenediol on the calcium metabolism of a man aged 24 who was bedridden with severe spondylitis ankylopoietica and calcification of the spinal ligaments. The patient was maintained on a low-calcium diet containing 160 mg. of calcium daily. Vitamin D (5,000 i.u.), cortisone, methylandrostenediol, and extra calcium were administered in varying combinations and amounts for periods of 2 to 3 weeks at a time.

On this low calcium intake the negative calcium balance was further depressed by cortisone. When the intake of calcium was raised by giving calcium phosphate and vitamin D, however, the calcium balance became positive in spite of the continued administration of cortisone; calcium retention was still further increased during a 21-day period during which methylandrostenediol was given, excretion of calcium in both the urine and faeces being reduced by the hormone. It is therefore suggested that to counteract the danger of osteoporosis in patients with Cushing's syndrome or those receiving prolonged treatment with ACTH or cortisone, calcium and vitamin D should be given freely, with, in addition, occasional short courses of methylandrostenediol. *C. L. Cope*

166. **Studies on the Metabolism of Adrenal Steroids in the Adrenogenital Syndrome**
A. M. BONGIOVANNI, W. R. EBERLEIN, and J. CARA. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **14**, 409–422, April, 1954. 3 figs., 15 refs.

The usual explanation of the production of the adrenogenital syndrome and of its amelioration by cortisone is that in this condition there is an inability of the adrenal cortex to synthesize the glucogenic corticoid (17-hydroxycorticosterone or hydrocortisone). This leads to an overproduction of adrenocorticotrophin by the pituitary gland in an effort to compensate for the deficiency. The resulting excess of adrenocorticotrophin stimulates adrenal androgen secretion, but cannot overcome the basic disorder. The administration of cortisone prevents this pituitary hypersecretion.

At the Johns Hopkins University School of Medicine, Baltimore, the authors have investigated the basic cause of the metabolic failure. They found that pregnanetriol was present in large amounts (up to 118 mg. daily) in the urine of 13 patients with congenital adrenal hyperplasia; the patients included subjects of both sexes ranging in age from 3 weeks to 16 years and one adult aged 30. This substance was undetectable or excreted in very small amounts (much less than 1 mg. daily) in normal subjects, though high values were found in 2 cases of adrenal tumour. The high excretion rate in the patients with adrenal hyperplasia was abolished when they were treated with cortisone. The intravenous administration of adrenocorticotrophin increased the excretion of pregnanetriol by the patients—particularly in 2 cases in which its excretion had been suppressed by cortisone—but had no such effect on subjects with normal adrenocortical function. Other differences were that the adrenocorticotrophin raised the level of 17-hydroxycorticoids in the blood of normal subjects, but did so only rarely in the patients, while the excretion of pregnanetriol by the patients was increased after administration of 17-hydroxyprogesterone, but was unaffected in the normal subjects.

These results led the authors to conclude that the basic disorder in the adrenogenital syndrome is a failure of the conversion of 17-hydroxyprogesterone to 17-hydroxycorticosterone in the adrenal cortex, and that this conversion is an essential step in the synthesis of the latter. The excess of 17-hydroxyprogesterone thus produced in the hyperplastic adrenal gland is excreted as pregnanetriol, just as excess progesterone is excreted as pregnanediol. (The authors hope to devise a simplified method for the routine determination of pregnanediol and pregnanetriol which may be useful in the diagnosis of those cases in which 17-ketosteroid excretion is only very slightly increased.) *Peter C. Williams*

167. **The Effect of Insulin on Nitrogen Retention in the Hypophysectomized Rat**
R. T. B. LAWRENCE, J. M. SALTER, and C. H. BEST. *British Medical Journal* [*Brit. med. J.*] **11**, 437–439, Aug. 21, 1954. 1 fig., 17 refs.

The senior author, with Salter, has reported (*Brit. med. J.*, 1953, **2**, 353; *Abstracts of World Medicine*, 1954, **15**, 161) that insulin promotes growth in hypophysectomized rats, the animals gaining weight owing to increases in protein, fat, and water. The finding of an increase in body protein led to the present detailed study at the University of Toronto of the effect of insulin on nitrogen retention, in which 8 hypophysectomized male rats (average weight 119 g.) received daily injections of increasing amounts of protamine zinc insulin for 7 days while receiving *ad lib.* a standard food mixture. Balance studies were carried out and the animals were killed on the 12th day.

Analysis of the carcases of the insulin-treated rats showed a great increase of nitrogen content compared with controls. During the period of insulin administration the balance studies showed that there was a marked increase in the absolute amount and percentage of nitrogen retained. There was also an increase of food intake and the body weight rose. When the insulin injections were stopped, nitrogen equilibrium was restored and the body weight fell. The loss of weight was due to loss of fat or water, or of both; no appreciable amount of protein was lost since in no case was there a significant negative nitrogen balance. These results confirm the

view that insulin promotes the synthesis of proteins and can function as a growth hormone in the absence of pituitary factors. *K. O. Black*

168. **The Lymphocytic Response as an Indicator of Relative Adrenocortical Insufficiency**
L. F. KUMAGAI and T. F. DOUGHERTY. *Endocrinology* [*Endocrinology*] **55**, 90–99, July, 1954. 3 figs., 8 refs.

In this article from the University of Utah, Salt Lake City, the authors describe experiments carried out on mice in order to further the understanding of the relationship between two previously observed phenomena concerning the lymphocytic system. These phenomena (which were previously described by the authors (*Endocrinology*, 1951, **48**, 691)) are that stress stimuli induce a lymphocytic response in adrenalectomized animals, and that adrenocortical hormones produce a lymphopenic response in the intact animal. Their experiments consisted in giving stress stimuli (in the form of histamine) to intact and adrenalectomized mice. They demonstrated that the degree of lymphocytosis produced by stress is inversely proportional to the amount of adrenocortical hormone available to the animal, this being shown by measuring the lymphocyte response after stress in adrenalectomized animals in which cortisone had been administered to replace the natural secretions of the adrenal glands.

The authors believe that in a state of relative adrenocortical insufficiency, as may occur in a chronic disease such as tuberculosis, the administration of a standard stress might produce a very poor lymphopenic response or even a lymphocytosis. Such a test, they suggest, might be used to assess the degree of impairment of adrenocortical function. *G. S. Crockett*

169. **Exophthalmos: its Relation to Adrenocortical Function.** [In English]
K. ATERMAN. *Acta endocrinologica* [*Acta endocr. (Kbh.)*] Suppl. 20, 1–59, 1954. 25 figs., bibliography.

DIABETES MELLITUS

170. **Diabetic Neuropathy: Controlled Therapeutic Trials**
C. R. SHUMAN and S. F. GILPIN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 612–617, June, 1954. 13 refs.

An attempt was made at the Temple University Hospital, Philadelphia, to assess the value of vitamin B_{12} (cyanocobalamin) and various other agents in the treatment of diabetic neuropathy in 37 cases. During an initial period of careful diabetic control with insulin and a diet supplying adequate protein and calories 12 of the patients obtained marked symptomatic relief and, in most instances, improvement in their physical signs, and were therefore excluded from the subsequent therapeutic trials. Vitamin B_{12} was given by intramuscular injection to 12 patients in doses of 10 to 1,000 μg. daily without benefit, and pregnant mammalian liver extract was similarly ineffective in 15 cases. Adenosine triphosphate, 25 mg., with aneurin, 20 mg., given intramuscularly twice daily for 2 to 4 weeks produced subjective improvement in 2 of 6 patients treated, whereas no improvement was observed in 4 patients treated with adenosine triphosphate, 25 mg., and pantothenic acid, 10 mg., intramuscularly daily for 3 weeks.
K. O. Black

171. **Dietary Fructose in Children with Diabetes Mellitus**
A. F. HARTMANN, H. J. WOHLTMANN, and A. F. HARTMANN, JR. *Journal of Pediatrics* [*J. Pediat.*] **45**, 27–50, July, 1954. 9 figs.

The authors have investigated, at the Washington School of Medicine, St. Louis, and the St. Louis Children's Hospital, the effects of incorporating fructose in the diet of diabetic children. Five children were selected because of good physical status and reasonable stability of the diabetic state. Diets were devised so that 15% of the total calories were derived from natural proteins (meat, eggs, and milk), 40% from natural fats, 20% from natural carbohydrate, and 25% from purified fructose, glucose, or sucrose.

The three variables in this diet, namely, the three sugars, were substituted in turn, but the amount of insulin required remained unchanged in 4 of the 5 children, and it was concluded that fructose exerted no insulin-sparing effect. In the 5th child an apparent insulin-sparing effect was eventually interpreted as being due to spontaneous improvement.
I. McLean Baird

172. **Are Diabetic Degenerative Complications Preventable?**
D. M. DUNLOP. *British Medical Journal* [*Brit. med. J.*] **2**, 383–385, Aug. 14, 1954. 1 fig., 19 refs.

In this review (which formed part of the author's Lumleian Lectures) from the University of Edinburgh, the author contrasts the two opposing points of view concerning diet in diabetes mellitus. He cites his own experience of allowing "free diet" to 50 diabetic patients who were followed up for 9 years. The results are described as "disastrous"—9 patients developed tuberculosis, 14 retinopathy, neuropathy, or renal complications, 3 patients had obesity and pruritus, 4 died from cardiovascular causes, and in only 9 cases (18%) were the results satisfactory. This low percentage has convinced the author once more of the necessity for strict dietetic control.

More recently he has examined a series of 167 diabetics with a view to assessment of their diabetic state, the degree of control being arbitrarily classified as good, fair, or poor. Only 27 of these patients (16%) were entirely free from complications, and such patients occurred nearly five times more frequently (33% compared with 7%) in the "good" than in the "poor" control group. Ophthalmic and renal complications were much more numerous in the poorly controlled group, but cardiovascular complications were present in 63% of all patients—an incidence and severity not affected by the degree of diabetic control. Although some diabetic complications may not be preventable by any

measures, the best chance is obtained by strict adherence to a diet containing not more than 200 g. of carbohydrate per day, all food being weighed, and regular periodical attendance at a diabetic clinic. As the author concludes: " it is most exceptional to encounter a well-controlled diabetic who has been made entirely responsible for his own treatment ". *I. McLean Baird*

173. **Treatment with Insulin Zinc Suspensions**
G. MELTON. *British Medical Journal* [*Brit. med. J.*] **2**, 448–449, Aug. 21, 1954. 5 refs.

A series of 52 cases of diabetes mellitus were treated with insulin zinc suspension [I.Z.S.]. All 16 new cases were satisfactorily stabilized on this preparation. Of the 36 patients transferred from treatment with older insulins, 26 were satisfactorily controlled by I.Z.S. alone, and 4 other cases reasonably well controlled by I.Z.S. mixtures. Six patients were restored to their previous insulin treatment because it had been more effective, and in some of them the diabetes had become markedly out of control whilst on I.Z.S.—[Author's summary.]

174. **The Protein-bound Carbohydrates in Serum from Diabetic Patients and the Relation to the Duration of Diabetes and the Vascular Complications**
G. H. NIELSEN and J. E. POULSEN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **1**, 70–78, June, 1954. 7 figs., 19 refs.

Some workers have reported an increase in the plasma level of protein-bound carbohydrates in patients with tuberculosis, cancer, and myocardial infarction. It has also been shown that the serum concentration of protein-bound carbohydrates is higher in diabetic patients with vascular complications than in diabetics with minimal complications. In a number of diabetic patients the present authors estimated the protein content of (*a*) serum, (*b*) precipitate after 50% saturation with ammonium sulphate, and (*c*) the filtrate after precipitation; the amount of glucosamine and of non-glucosamine carbohydrate present in the three serum-protein samples was also measured. The protein content was determined by the Kjeldahl method described by Andersen and Jensen, the glucosamine content by the method of Sorenson as modified by Blix, and the non-glucosamine content by the orcinol method.

In diabetics with renal and retinal lesions there was a decrease in the serum total protein content proportional to the degree of the severity. In patients with uncomplicated diabetes no significant change was observed. The values for non-glucosamine protein-bound carbohydrate were almost the same in non-diabetic controls as in patients with uncomplicated diabetes, the fraction being uninfluenced by the duration of the diabetes. The carbohydrate content of the ammonium-sulphate precipitated protein was markedly raised in the albumin fraction in patients with vascular complications. A slight increase was observed in the amount of glucosamine present in the serum total protein of patients with diabetes as compared with non-diabetics, and there was a higher percentage of glucosamine in the albumin fraction in diabetic patients with vascular complications.

With strict diabetic treatment in hospital of a group of poorly-controlled patients with vascular complications the values for serum total protein, albumin, and carbohydrate and the percentage of carbohydrate in the three protein samples showed a trend towards the normal. The authors were unable to find any correlation between the level of protein-bound carbohydrate and the blood sugar concentration at the time the blood samples were taken. They consider that, until a more refined technique permits isolation of some glycoprotein characteristic of diabetes, the changes in plasma protein values in this disease must be considered to be the result of a non-specific reaction of the organism. *J. Lister*

175. **The Incidence of Vascular Disorders in Diabetics Surviving 15–25 Years after Onset of the Disease**
K. LUNDBAEK. *Danish Medical Bulletin* [*Dan. med. Bull.*] **1**, 67–70, June, 1954. 1 fig., 3 refs.

With a view to determining the incidence of vascular disorders in long-standing cases of diabetes, the author, at Kommune-hospitalet, Aarhus, Denmark, carried out an investigation among 165 unselected patients who had been suffering from diabetes for more than 15 years.

Two-thirds of the patients had simple diabetic retinopathy; 6% had retinitis proliferans; but blindness due to diabetic eye disease was found in only 3%. No significant difference in incidence was found between the young, middle-aged, and older age groups. Some form of chronic nephropathy, which was defined as an abnormal number of erythrocytes or casts in the urine combined with hypertension, proteinuria, or oedema, occurred in 25% of the cases. The features of the fully-developed Kimmelstiel–Wilson syndrome with massive oedema were seen in only 6% of the cases.

Coronary arterial disease was found in 65% of patients over 65 years of age; it was less frequently seen in younger age groups, though 13% of long-standing diabetics under 40 had symptoms or signs of coronary arterial disease. In these younger patients there was also evidence of severe retinal and renal changes. Peripheral vascular disease was more common in older patients—49% of patients over 60, but only 5% of those under 40, being affected. Objective signs of neuropathy were present in 5% of the patients, but subjective neurological symptoms suggesting neurological disturbances were frequent.

In the discussion the author expresses the view that the vascular lesions in long-standing diabetes are the expression of a diabetic angiopathy occurring in association with atherosclerosis and medial sclerosis. Retinopathy and nephropathy occur equally in young and old, but the incidence of coronary arterial disease and of peripheral vascular disease increases with age. The absence of any correlation between age and diabetic retinopathy and nephropathy would suggest that these complications are purely diabetic.

The author suggests that in coronary arterial disease of diabetics there is a mixture of diabetic angiopathy and atherosclerosis, whereas in the peripheral vascular disease there is a medial sclerotic element.

J. Lister

The Rheumatic Diseases

176. **Intramuscular Benzathene Penicillin in the Prophylaxis of Streptococcal Infection in Rheumatic Children** C. B. PERRY and W. A. GILLESPIE. *British Medical Journal* [*Brit. med. J.*] **2**, 729–730, Sept. 25, 1954. 6 refs.

The object of the investigation described in this paper from the United Bristol Hospitals (University of Bristol) was to determine the value of benzathine penicillin (N:N′-dibenzylethylenediamine di (benzylpenicillin)) in the prophylaxis of streptococcal infection following rheumatic fever. To 22 rheumatic children, 15 of whom had been persistent carriers of Group-A haemolytic streptococci for 4 to 9 weeks, the antibiotic was given intramuscularly at monthly intervals in doses of 1·5 mega units each; one child received 5 doses, 7 received 4 doses, 6 received 3 doses, 5 received 2 doses, and 3 received only one dose. The serum penicillin level was estimated 4, 11, 18, and 25 days after the injection. Most of the injections caused local tenderness for 24 to 48 hours, and in 18 out of 67 instances slight fever was noted on the day after injection. On the 4th day the serum concentration of the drug ranged from 0·24 to 0·025 unit per ml., with an average concentration of 0·08 unit per ml.; on the 11th it ranged from 0·14 to 0 unit per ml. (average 0·043); on the 18th day from 0·1 to 0 unit per ml. (average 0·029); and on the 25th day from 0·07 to 0 unit per ml. (average 0·012).

Within 4 days Group-A streptococci were eliminated from the throats of all except one of the 15 persistent carriers. New infections were almost, though not completely, prevented. *R. S. Illingworth*

177. **The Treatment of Chronic Arthritis with a Combination of Cobra Venom, Formic Acid, and Silicic Acid** K. D. BRYSON. *American Surgeon* [*Amer. Surg.*] **20**, 751–755, July, 1954. 2 refs.

The author describes the treatment of a series of 466 consecutive cases of chronic arthritis (excluding 150 in which the course was not completed) with "nyloxin", a preparation containing cobra venom, formic acid, and silicic acid, given by subcutaneous injection in doses increasing from 1 to 3 ml. Treatment was usually given at weekly intervals at first, then less frequently as control of symptoms was obtained, until eventually in most cases the patient received only a maintenance injection every 3 months. The patients are classified in three broad diagnostic groups—osteoarthritis, rheumatoid arthritis, and mixed types—the numbers in these groups being 344, 74, and 48 respectively. The results as assessed by the physician after consideration of all the relevant factors were "satisfactory" in 426 cases (91·4%) and "unsatisfactory" in 40 (8·6%). The patients' own opinions on their condition before, during, and after treatment are analysed separately and here again the results show a high proportion of successes; for instance, of 94 patients reporting 6 months to 5 years after cessation of treatment, 88 (93·6%) said that their condition remained satisfactory. The author also notes that the patients' general health was improved, often with a rise in the haemoglobin level, and that hypertension, where present, was reduced.

[It is unfortunate that insufficient clinical details are given in this paper to enable the reader to assess the value of this treatment.] *K. C. Robinson*

178. **Evaluation of the Bryson Treatment of Arthritis** W. R. LUMPKIN and W. M. FIROR. *American Surgeon* [*Amer. Surg.*] **20**, 756–759, July, 1954. 2 refs.

An investigation was carried out at the Maryland General Hospital, Baltimore, into the claim of Bryson [see Abstract 177] that a mixture of cobra venom and silicic and formic acids was effective in the treatment of chronic arthritis. Three solutions were prepared for subcutaneous injection: (A) containing formic acid only; (B) containing all three ingredients in the proportions used by Bryson; and (C) a mixture of formic and silicic acids. The patients, who were classified as having either rheumatoid or hypertrophic arthritis (the latter predominating), were given weekly injections of one or other of these preparations in increasing doses, the interval being later extended gradually as described by Bryson. The results were as follows: 10 patients had Solution A, and one responded; 61 had Solution B, and 52 responded; and 10 had Solution C, and 8 responded (though the degree of improvement was thought to be less than with Solution B). A response was defined as the subsidence or cessation of pain, swelling, and stiffness in the affected joints, and improvement in general health. The authors conclude that Bryson's treatment gives substantial relief of symptoms in more than 80% of cases of chronic arthritis. *K. C. Robinson*

179. **The Serological Differential Diagnosis of Certain Forms of Chronic Rheumatism.** (Zur serologischen Differentialdiagnostik einzelner Formen des chronischen Rheumatismus)
H. SEIFERT and H. TICHY. *Zeitschrift für Rheumaforschung* [*Z. Rheumaforsch.*] **13**, 133–151, June, 1954. 48 refs.

In a study carried out at the Institute of Rheumatology, Dresden, the following serological tests were carried out on 228 rheumatic patients: (1) determination of antistreptolysin titres; (2) the Rose agglutination test, using sensitized sheep erythrocytes; (3) the Paul–Bunnell test, using fresh, untreated sheep erythrocytes; (4) the Svartz and Schlossmann agglutination test, using absorbed serum and sensitized sheep cells; (5) the L-agglutination test, based on the agglutinable antigen of β-haemolytic streptococci (method of Nicholls and Stainsby).

From the results of these tests the authors conclude that high titres in Tests 2 and 5 together with low titres

in Tests 1 (antistreptolysin), 3, and 4 are serologically diagnostic of rheumatoid arthritis. In cases of ankylosing spondylitis, antistreptolysin titres were particularly high and all the other tests gave low readings. It is claimed that serological tests are of practical value in rheumatoid arthritis, since by their use a diagnosis can frequently be made before the appearance of the characteristic clinical changes and of the accelerated erythrocyte sedimentation rate.

[The original paper should be consulted for the various serological techniques, which are given in some detail.]

D. Preiskel

180. **Low Diastolic Pressure as a Clinical Feature of Rheumatoid Arthritis and its Possible Etiologic Significance** L. W. TURNER and J. LANSBURY. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **227**, 503–508, May, 1954. 1 fig., 9 refs.

The blood-pressure readings of 320 patients with rheumatoid arthritis of at least 9 months' duration admitted to Temple University Hospital, Philadelphia, were compared with the average values published for a series of 5,540 presumably normal subjects; in the case of the patients the pressure was determined on admission to hospital, in order to discount the hypotensive effect of subsequent bed rest.

The results showed that the average blood pressure (by decades) in the arthritic group was significantly lower than in the control group, ranging from 115/74 to 127/75 mm. Hg in the former, and from 120/77 to 166/92 mm. Hg in the latter. The average diastolic pressure of the arthritic patients remained virtually unchanged through all age decades from 20 to 70 years at about 75 mm. Hg, whereas that in the normal group rose with age; the differences in the systolic pressures were less striking. Only 5% of the rheumatic cases were considered to be hypertensive.

The authors conclude that hypotension [*sic*] is a constant feature of rheumatoid arthritis. They discuss at some length what they consider to be the aetiological implications of their observations in the light of reports that the use of hypotensive drugs (particularly hydrallazine) may precipitate clinical syndromes resembling rheumatoid arthritis, disseminated lupus erythematosus, and scleroderma. *Kathleen M. Lawther*

181. **Colloidal Gold Sulphide in the Treatment of Rheumatoid Arthritis.** (Le sulfure d'or colloïdal dans la thérapeutique de la polyarthrite chronique évolutive) J. FORRESTIER and F. THÉVENOZ. *Presse médicale* [*Presse méd.*] **62**, 1056–1057, July 10, 1954. 1 fig., 1 ref.

The colloidal preparations of gold salts have never proved satisfactory in the treatment of rheumatoid arthritis mainly owing to their low content of metallic salts. A new preparation has, however, recently been introduced in the form of colloidal gold sulphide ("aurolsulfide"), which contains a higher proportion of active gold. This preparation has been found by the authors to be highly effective, and in their experience has been better tolerated by the patient than are the "classic gold preparations".

Of 23 patients with chronic rheumatoid arthritis, 11 responded in an extremely satisfactory fashion, 7 were appreciably benefited, and only 5 showed no improvement. In all the cases which benefited the erythrocyte sedimentation rate diminished *pari passu* with the clinical improvement. The authors consider this new preparation of gold to represent an advance in chrysotherapy.

W. S. C. Copeman

182. **Observations on the Treatment of Rheumatoid Arthritis by Transfusions of Blood from Pregnant Women** C. JOSEPHS. *British Medical Journal* [*Brit. med. J.*] **2**, 134–135, July 17, 1954. 5 refs.

An investigation was undertaken at Staincliffe General Hospital, Dewsbury, Yorkshire, to compare the effects on rheumatoid arthritis of transfusions of blood from pregnant women and of similar transfusions from men and non-pregnant women. Transfusions of 300 ml. were given weekly and the cases followed up for 6 to 18 months.

Of the 53 cases given blood from pregnant donors, 19% are stated to have shown marked subjective and objective improvement, as compared with 13% of 45 cases receiving blood from men and non-pregnant women.

The author concludes that in rheumatoid arthritis transfusion of blood from pregnant donors produces improvement similar to that resulting from transfusion of blood from non-pregnant donors, but does not produce remissions comparable to those observed during pregnancy. *H. F. Turney*

183. **Effects of Phenylbutazone in Gout** H. P. JOHNSON, E. P. ENGLEMAN, P. H. FORSHAM, M. A. KRUPP, T. W. GREEN, and A. GOLDFIEN. *New England Journal of Medicine* [*New Engl. J. Med.*] **250**, 665–670, April 22, 1954. 4 figs., 12 refs.

The authors report upon the use of phenylbutazone in the treatment of 10 patients with acute gouty arthritis and 16 cases of chronic gout at the Veterans Administration Hospital, San Francisco. The drug was given either by intramuscular injection in 20% aqueous solution or by mouth in enteric-coated capsules. The daily dose in the acute cases was 0·8 to 1 g., but varied in the chronic cases from 0·4 to 1 g. Subjective relief was obtained in 19 out of 20 attacks of acute gout, and the number of exacerbations was effectively reduced in the chronic cases. Toxic symptoms, however, occurred in 9 of the 16 cases of chronic gout. The majority of these occurred during the first few weeks of treatment, but the fact that some occurred later suggests that the drug should not be used as a routine in chronic gout unles all other forms of treatment have failed.

The exact mode of action of the drug is not known; it lowers the blood uric acid level and also diminishes urinary excretion of uric acid, 17-hydroxycorticoids, and sodium. The authors do not advocate the routine use of phenylbutazone in the treatment of gout; they merely indicate its therapeutic effect and recommend consideration of its use in cases of gout resistant to other established forms of treatment. *R. E. Tunbridge*

Neurology and Neurosurgery

184. **The Use of Soviet Curariform Preparations in the Treatment of Nervous Diseases.** (Применение отечественных курареподобных препаратов в клинике нервных болезней)
N. A. KRŸSHOVA, M. A. ZHILINSKAYA, K. M. KOVALENKOV, and E. A. BŸCHENKOVA. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 579–582, July, 1954. 6 refs.

The authors report the results of a clinical trial with a curare-like preparation " K2 " (extracted from plants growing in the U.S.S.R.) in the treatment of various neurological conditions. The drug was given initially in doses of 25 mg. daily by mouth increasing to 50 mg. three times daily, each course lasting 10 days and being sometimes repeated after a period of 7 to 10 days. The 37 patients in the series, all of whom had previously been unsuccessfully treated by other methods, included 26 with extrapyramidal and 11 with pyramidal motor disturbances. The results of the treatment were encouraging in most of the cases (but not in disseminated sclerosis), and the improvement was maintained in some of them for several months. *L. Crome*

185. **Studies in Myasthenia Gravis. Preliminary Report on Therapy with Mestinon Bromide**
K. E. OSSERMAN, P. TENG, and L. I. KAPLAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 961–965, July 10, 1954. 14 refs.

Following reports that " mestinon " (pyridostigmine bromide) is superior to neostigmine in the treatment of myasthenia gravis, a trial was made with this drug in 20 cases of the disease (4 in men and 16 in women) at the Mount Sinai Hospital, New York. Five of the cases were severe, 9 moderate, and 6 mild.

For purposes of comparison these patients were first given neostigmine until the most effective dose was reached. This ranged from 75 to 540 mg. daily according to the severity of the disease. Patients were then given a thorough clinical examination and subjected to serial edrophonium (" tensilon ") testing. (Edrophonium is a cholinergic drug the response to which reveals the effects of the drug under trial.) Mestinon was then substituted for the neostigmine, 60 mg. being given for every 15 mg. of neostigmine. Clinical assessment and edrophonium testing were then carried out as before. Most patients received mestinon therapy for 7 months.

The effects of mestinon were found to last only half an hour longer than those of neostigmine. The former was more effective in the relief of the small muscles innervated by the cranial nerves, but a few patients complained that they did not get the " lift " they experienced after taking neostigmine. There were fewer side-effects with mestinon, both in cases in which it had a greater antimyasthenic effect and in those in which it did not. Of the 20 patients, 15 found mestinon more effective than neostigmine; in 9 of these the results were excellent. The most remarkable results, however, were obtained in 2 cases with myasthenic crises.

The authors consider that the most beneficial effect of this treatment was the marked decrease in side-reactions, but that further evidence of the superiority of mestinon over neostigmine in the treatment of myasthenia gravis is needed before it can be recommended as the drug of choice. *N. S. Alcock*

186. **ACTH and Cortisone in the Treatment of Multiple Sclerosis.** [In English]
G. VON REIS, E. SAHLGREN, and B. JÖNSSON. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] **28**, 429–438, 1954. 9 refs.

In an investigation at the Södersjukhus, Stockholm, 51 patients with disseminated sclerosis, most of whom had had symptoms for less than 2 years, were treated with ACTH or cortisone. Improvement is claimed in 74% and almost complete recovery from symptoms in 48%. [Unfortunately there are no control series and no specific measurements. For example, although improvement in vision is claimed in one group of patients, the precise effect on visual acuity or field defects is not mentioned. No conclusions should be drawn from the results of this work.] *Hugh Garland*

187. **Homonymous Hemianopia in Multiple Sclerosis**
M. CHAMLIN and L. M. DAVIDOFF. *Neurology* [*Neurology*] **4**, 429–437, June, 1954. 6 figs., 16 refs.

A study of the literature showed that homonymous hemianopia in disseminated sclerosis is extremely rare (in contrast to the frequent involvement of the optic nerves). Indeed the authors could find only 3 previously reported cases, to which they now add a further 4 seen at the Mount Sinai Hospital, New York, since 1951. The diagnosis of disseminated sclerosis was made on clinical grounds only, but appeared to be reasonably certain. A feature of 3 of their 4 cases, as well as the 3 described in the literature, was the presence of a dense paracentral homonymous defect, suggesting that the lesion was near the occipital cortex. Of the 3 patients that could be followed up, all showed spontaneous remission. *Donald McDonald*

188. **Ischaemic Lateral Popliteal Nerve Palsy**
F. R. FERGUSON and L. A. LIVERSEDGE. *British Medical Journal* [*Brit. med. J.*] **2**, 333–335, Aug. 7, 1954. 8 refs.

In this paper from Manchester Royal Infirmary (Manchester University) the authors describe 9 cases in which sudden onset of an external popliteal nerve palsy was associated with evidence of either thrombosis or embolism of the femoral or popliteal artery. In some of the cases there was evidence of a partial lesion of the internal popliteal nerve. It is pointed out that the external

popliteal nerve is more vulnerable to ischaemic lesions than the internal because of its very limited blood supply. The prognosis as regards local function in these cases is good and recovery is the rule. [This syndrome differs in many respects from external popliteal nerve palsy resulting from compression, the chief differences being the frequent pain in the former and evidence of involvement of the internal popliteal nerve and of femoral or popliteal thrombosis. There is an unfortunate misprint in the fifth line from the end of the second paragraph, where " arteritis " appears as " arthritis ".]

Hugh Garland

189. **Electroencephalographic Studies of the Encephalopathies. III. Serial Studies in Measles Encephalitis**

L. L. LEVY and E. ROSEMAN. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **88**, 5–14, July, 1954. 7 figs., 12 refs.

From the Louisville General Hospital 10 cases are described in which electroencephalograms (EEGs) recorded during encephalitis complicating an attack of measles showed generalized slow activity which, in these circumstances, is considered to be indicative of acute encephalitis unless the record is made shortly after the occurrence of an epileptic attack. Conversely the absence of such activity makes it unlikely that encephalitis is present. Serial EEGs showed parallelism between the amount of slow activity and the severity of the disease, but the degree of abnormality did not appear to be related to the final prognosis. In some cases there was an apparently permanent dysrhythmia after recovery which, however, was not directly related to any mental or behavioural disturbance. *W. A. Cobb*

190. **Metastatic and Primary Intracranial Tumors of the Adult Male**

K. M. EARLE. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath.*] **13**, 448–454, July, 1954. 1 fig., 6 refs.

In a series of 3,946 consecutive autopsies for a 4-year period at the Veterans Administration Center, Los Angeles, California, there were 1,498 adult males with malignant neoplasm. The brains were removed and studied in all but 69 of these cases. Metastasis to the brain was found in 167 cases (11% of all tumors), and 99 cases had a primary intracranial tumor. Bronchogenic carcinoma was the most common source of metastatic brain tumors (57% of all metastatic tumors). Other primary sources were represented by: malignant melanoma in 7·1%; large intestine in 6·5%; kidney in 4·6%; and testis in 4·6% of the cases. None of the other primary sources were over 3% of all metastatic tumors.

The metastases to the brain were found to be more often multiple than solitary. Solitary metastases were more common in one of the cerebral hemispheres (68%) than in the cerebellum (28%) or brain stem (4%). There was no significant predominance of the two cerebral hemispheres. When the metastases were multiple, they involved both the cerebrum and cerebellum in about half of the cases; and involved both cerebral hemispheres, but not the cerebellum in about one-third of the cases.

Glioblastoma multiforme was the most common primary intracranial neoplasm in this autopsy series of male veterans.—[Author's summary.]

191. **Cerebrospinal Fluid Changes following Closed Craniocerebral Injuries**

R. A. DAVIS. *Neurology* [*Neurology*] **4**, 422–428, June, 1954. 3 refs.

In the 2 years July, 1951, to July, 1953, out of 546 admissions to the neurosurgical ward of the U.S. Naval Hospital, Bethesda, Maryland, there were 222 cases of head injury, of which 162 were of the closed type. It is on 43 cases of the latter group that the present study is based; in none of them was the skull fractured and in all cases the period of unconsciousness had been at least 5 minutes, so far as could be ascertained.

In most cases the protein content of the cerebrospinal fluid (C.S.F.) was raised, being over 45 mg. per 100 ml. in 18 cases, notably in those showing neurological signs, and in 6 of the latter cases the C.S.F. contained more than 100 erythrocytes per c. mm. Patients who had had long periods of unconsciousness also tended to have a high C.S.F. protein content. The level of sugar in the C.S.F. was also raised in 18 patients (to above 80 mg. per 100 ml.), the value varying inversely with the duration of unconsciousness. There was no correlation between raised intracranial pressure and the severity of the injury; the average intracranial pressure for the whole group was 187 mm. of water, 180 mm. being taken as the upper limit of normal. Similarly, the presence of erythrocytes in the C.S.F. or increase in its chloride content had no diagnostic or prognostic value.

The findings are analysed in considerable detail in relation to neurological defect, state of consciousness, symptomatology, and sequelae. [The original paper should be consulted by specialists in this field.]

Donald McDonald

192. **The Problems of Cerebral Atrophy in the Adult**

E. D. FISHER and L. B. MANN. *Bulletin of the Los Angeles Neurological Society* [*Bull. Los Angeles neurol. Soc.*] **19**, 105–113, June, 1954. 23 refs.

After reviewing the relevant literature the authors criticize earlier published work on cerebral atrophy because the material has been drawn from mental hospitals rather than from medical practice. In their experience only a minority of patients with cerebral atrophy show any degree of dementia.

At the County Hospital and the White Memorial Hospital, Los Angeles, 200 cases of cerebral atrophy were found, by encephalography in 159 and at necropsy in 41. Of 55 patients aged 60 to 94 years, only 22 showed " mental deterioration or senile psychosis ". Among 100 aged 25 to 55 years the incidence of atrophy was highest in the age group 35 to 44; in only 7 of these was there evidence of mental deterioration. Convulsions occurred in 74 cases and in 102 there were various focal neurological manifestations. Atypical neurosis was considered to be a suspicious sign. Neither examination

of the cerebrospinal fluid nor electroencephalography was helpful in diagnosis.

No evidence is offered concerning the pathology of the cerebral atrophy, but the authors believe that the condition in their cases was not related to either Pick's or Alzheimer's disease.

[It all depends, it would seem, on what one means by cerebral atrophy.] *L. G. Kiloh*

193. **Spontaneous Occlusion of the Internal Carotid Artery**

E. H. Feiring. *Neurology* [*Neurology*] **4**, 405–421, June, 1954. 9 figs., 36 refs.

The author describes 7 cases of spontaneous occlusion of the internal carotid artery which were found among a total of some 500 patients being investigated for suspected intracranial tumours or vascular anomalies at the Beth Israel and Mount Sinai Hospitals, New York. In 5 of the cases a diagnosis of intracranial tumour had already been made, but the true diagnosis was made in all cases by angiography; in no case could the lesion be confirmed at necropsy, although 2 of the patients died.

All 7 patients were men, ranging in age from 48 to 63. The duration of the condition ranged from 2 months to 5 years and the course had been progressive in 4 cases and episodic and fluctuating in the others. All suffered from hemiparesis, most of them from visual-field defect or actual loss of sight in one eye and, when the dominant hemisphere was involved, from disturbances of the speech function. Headache was a prominent feature in only 2 cases, and focal seizures occurred in 2 cases. The site of occlusion was close to the bifurcation of the common carotid artery in 5 cases and in the intracranial portion of the artery in the other 2. Changes were observed in the pneumo- and electro-encephalograms but these were not of diagnostic value. Therapy was attempted in only 2 cases, dicoumarol being administered; in one, however, it had to be discontinued because of haemorrhagic symptoms, but the other patient improved considerably and later returned to work. The condition is fully discussed in relation to other series of cases reported in the literature. *Donald McDonald*

CEREBRAL INFECTIONS

194. **Recent Experience of Encephalitis in Childhood**

E. G. Brewis. *British Medical Journal* [*Brit. med. J.*] **1**, 1298–1302, June 5, 1954. 12 refs.

Since 1943 at three hospitals associated with the University of Durham 93 cases of " encephalitis in childhood " have been seen, this term being used for the classic symptoms or signs of disturbed cerebral function in a previously healthy child, which, after exclusion of bacterial infection, vascular disorders, and poisoning, are presumed to be the result of non-suppurative disorder of the brain. The author has attempted a classification, based entirely on symptoms and the clinical course of the disease, according to which he recognizes " four main patterns of illness ". Cases illustrative of each type are described, including, in some instances, results of examination of the cerebrospinal fluid (C.S.F.) and, in some fatal cases, the necropsy findings. No constant relationship was found between the clinical picture and the aetiology and pathology of the disease.

The cases were classified as follows. Type 1, 28 cases, with sudden onset, convulsions, and unconsciousness; death (in 9 cases) or return to consciousness occurred generally in 2 or 3 days. There were 19 cases of unknown aetiology, 3 associated with measles, 4 with pertussis, one with mumps, and one with mononucleosis. Type 2, 15 cases, with acute onset, a somnolent phase, and paralyses. The only aetiological association in this group was an outbreak of poliomyelitis. Pleocytosis in the C.S.F. was the rule. Only 5 patients failed to show some lower motor neurone weakness, while pyramidal involvement and mental changes were observed in a few cases. There was one death in this group. Type 3, 9 cases, with insidious onset developing into continuous choreiform movements resembling athetosis. The illness in these patients was prolonged and locomotor sequelae were frequent. There was no special aetiological association, and post-mortem changes were surprisingly scanty. Two patients in this group died. Type 4, 17 cases, in which there was a somnolent and lethargic illness with spasticity and retardation, the illness resembling encephalitis lethargica. Of the 17 cases, 5 were of unknown aetiology, 7 were associated with measles, 3 with pertussis, one with rheumatic fever, and one with rubella. There were 2 deaths. The remaining 24 cases, in which there were miscellaneous symptoms, could not be placed in any one of these categories.

[This is a detailed and interesting presentation of the varied and complex symptoms seen in children suffering from " encephalitis ", as defined by the author. It is not clear that the classification furthers research or that it is an advance on others based on either aetiology or pathology, however unsatisfactory these last two may be. The author claims that the classification offers " guidance to the practitioner in giving a prognosis "; this is doubtful, since so many cases are of no special type and the signs and symptoms in the four groups often overlap. Frequency of convulsions, persistence of focal brain damage, and deep or long coma will always be recognized as evidence of severity and as indicating a poor prognosis, whatever the classification adopted.] *L. J. M. Laurent*

195. **Encephalitis during an Epidemic of Influenza.** [In English]

L. Crome. *Monatsschrift für Psychiatrie und Neurologie* [*Mschr. Psychiat. Neurol.*] **128**, 159–179, Sept., 1954. 10 figs., 49 refs.

196. **Pyogenic Meningitis**

G. D. W. McKendrick. *Lancet* [*Lancet*] **2**, 510–512, Sept. 11, 1954. 2 figs., 12 refs.

In this paper 107 consecutive cases of pyogenic meningitis admitted to Ham Green Hospital, Bristol, during 1948–53 are reviewed. The author points out that patients with purulent meningitis present with similar symptoms irrespective of the aetiology, and that there

are three outstanding factors which affect a given patient's chance of recovery: (1) the speed with which the presence of meningitis is discovered; (2) the type of meningitis present; and (3) the treatment given. Early recognition of the meningitis depends on examination of a direct film made from the cerebrospinal fluid, but treatment should not be delayed until the results of culture are known.

The types of meningitis and the number of deaths in this series were as follows:

Type of Meningitis	No. of Cases	Deaths
Meningococcal	49	—
Pneumococcal	30	2
Haemophilus influenzae	17	1
Staphylococcal	5	2
Streptococcal	1	1
Proteus vulgaris	1	—
Mixed	1	1
Unknown	3	—
Total	107	7

The treatment of meningococcal meningitis followed recognized lines. A soluble sulphonamide (usually sulphadimidine) was given intramuscularly in full doses until vomiting ceased. This was followed by " sulphatriad " (sulphadiazine, sulphathiazole, and sulphamerazine) in full doses. After 5 days a reduced dose was given for a further 2 days, the total course lasting 7 days. Penicillin was not given as a routine, but all patients in coma and those with clinical evidence of septicaemia received procaine penicillin, 300,000 units, with crystalline penicillin, 100,000 units, 12-hourly for 2 to 5 days. [Treatment in the cases of pneumococcal meningitis is described in another paper by the same author (see Abstract 197).]

The treatment of *H. influenzae* meningitis consisted in intramuscular injection of streptomycin in full doses for 10 to 14 days, intrathecal injection of streptomycin, 50 to 100 mg. daily (according to age) for 10 days, and oral administration of sulphadiazine in full doses for 7 days. A limited experience with chloramphenicol in this type of meningitis was not encouraging, and no conclusion was arrived at as to the treatment of choice.

Staphylococcal meningitis was treated with penicillin and sulphonamides.

In the discussion it is pointed out that many factors affect the mortality in pyogenic meningitis, but the presence of infective foci, except intracranial and epidural abscesses, has little effect on the prognosis. The possibility of localized pus in or around the brain or spinal cord must be borne in mind. It is considered that in the present series 2 deaths might have been averted had the abscesses been discovered and drained.

Early diagnosis is considered the most important factor, so that lumbar puncture should be performed on the slightest suspicion of meningeal irritation. If the cerebrospinal fluid is turbid at the first puncture, penicillin is given intrathecally, adults receiving 20,000 units and children a smaller dose according to age. This is said to be of value partly in saving time if pneumococcal or staphylococcal meningitis is present, and partly in saving the patient from another lumbar puncture if intrathecal injection of penicillin is indicated.

J. MacD. Holmes

197. **Pneumococcal Meningitis**

G. D. W. McKENDRICK. *Lancet* [*Lancet*] **2**, 512–513, Sept. 11, 1954. 1 fig., 11 refs.

The author reviews 35 cases of pneumococcal meningitis admitted to Ham Green Hospital, Bristol, during the period 1947–53. [These include the 30 cases referred to in the paper abstracted above (Abstract 196).] The ages of the patients ranged from 7 months to 71 years. Coma on admission did not seem to be necessarily of poor prognostic significance. In 7 cases the patient was admitted in a recurrent attack. There were 3 deaths in the series.

After pointing out that pneumococcal meningitis is often a secondary disease, the author lists the primary lesions in these cases as follows: otitis media, 13 cases; pneumonia, 3; sinus infection, 2; skull defects, 3; unknown, 14. In 2 cases there was a history of head injury within the previous month, radiography of the skull revealing linear fractures. One patient had had a previous attack of meningitis treated elsewhere 12 months earlier, followed by a fascial graft for cerebrospinal-fluid rhinorrhoea. One of the fatal cases was due to infection with a penicillin-resistant pneumococcus, an event which, the author considers, must be very rare.

All the patients received the same basic treatment, although there were variations in the amount of penicillin given intramuscularly. Routine treatment consisted in intramuscular injection of 200,000 units of crystalline penicillin 4-hourly for 10 to 14 days, intrathecal injection of 20,000 units of penicillin daily for 10 days, and a sulphonamide—either sulphadiazine or " sulphatriad " —in full doses by mouth for 7 days. A sulphonamide was given by intramuscular injection until vomiting ceased. The author is of the opinion that intrathecal administration of penicillin is necessary in pneumococcal meningitis for at least 7 days in addition to the intramuscular injection of penicillin and sulphonamides.

J. MacD. Holmes

EPILEPSY

198. **Isolated Fear. A Temporal Lobe Aura**

D. MACRAE. *Neurology* [*Neurology*] **4**, 497–505, July, 1954. 4 figs., 19 refs.

The author discusses cases of epilepsy in which fear occurs as an aura. Many epileptic patients may experience fear as the result of an unpleasant aura and the realization that a seizure is imminent; others may experience fear in isolation as a true " aura of terror ", irrespective of prevailing mood, thought content, or situation. It is with this second group that the present paper deals. Such isolated fear is brief in duration and ends abruptly if it is not followed by a seizure. It may be associated with recognized auras such as hallucinations of smell and abnormal psychic states.

The author describes 7 cases and discusses the nature and situation of the verified cerebral lesion in these and in 3 cases previously reported by others. The lesions included aneurysm, vascular sclerosis, and neoplasm, and the site varied from the frontal and temporal to the parieto-occipital lobes of either hemisphere. Electroencephalographic tracings, when available, were more consistent in showing a temporal-lobe focus, regardless of the site of the gross lesion. The author concludes that the aura of isolated fear has a focal significance, and indicates abnormal activity on the medial aspect of the temporal lobe on either side. *J. B. Stanton*

199. **Epileptic Sleep Terrors**
B. FÚSTER, C. CASTELLS, and M. ETCHEVERRY. *Neurology* [*Neurology*] **4**, 531–540, July, 1954. 10 refs.

Two types of " sleep terror ", those of epileptic origin and those of neurotic or banal origin, are discussed, and the electroencephalogram (EEG) in a group of patients so afflicted is described. Investigation of the incidence of sleep terrors among 228 epileptic patients and 139 children without a family history of epilepsy showed that 52 of the former and 13 of the latter had sleep terrors. Two types of sleep terror were thus distinguished: (1) banal sleep terrors—that is, terrifying nightmares without amnesia—occurring in those with a normal EEG and without a family history of epilepsy; and (2) epileptic sleep terrors in which the patient was unconscious and for which there was amnesia. Analysis of the EEG tracings showed a relationship between sleep terrors and the existence of abnormal discharges in the parieto-temporo-occipital region. The authors refer to a case described in a personal communication by Walker in which, after excision of the part of the parieto-temporo-occipital lobe which was the site of an epileptic EEG focus, the sleep terrors disappeared. Differentiation of epileptic sleep terrors from other automatisms, such as sleep-walking, by means of the EEG is discussed.

[It is interesting to compare the conclusions concerning the focal significance of sleep terrors with those of Macrae concerning the aura of isolated fear in the waking state (see Abstract 198).] *J. B. Stanton*

200. **Primidone in the Treatment of Epilepsy**
J. B. LYONS and L. A. LIVERSEDGE. *British Medical Journal* [*Brit. med. J.*] **2**, 625–627, Sept. 11, 1954. 2 figs., 9 refs.

The authors, at the Manchester Royal Infirmary, studied the therapeutic effect of primidone (" mysoline "; 5-ethyl-5-phenyl-hexahydropyrimidine-4:6-dione) in 44 cases of epilepsy, the period of observation ranging from 3 to 14 months. The dosage varied from 0·5 to 2·5 g. daily, the majority of patients requiring 1 to 1·5 g. daily divided into 3 or 4 doses.

Of 42 patients maintained on this treatment, 28 had some improvement, 13 were unaffected, and one became worse. Of the 28 patients who were improved, 12 had complete relief from attacks, 9 noted a 75% reduction in their frequency, and 7 a reduction varying from 25 to 75%. The frequency and severity of myoclonic jerks were unaffected in 2 patients. Of the 6 cases in which electroencephalograms were taken before and after treatment, in 2 an improvement in the recorded pattern was found; both patients had obtained complete relief as the result of treatment.

Toxic side-effects noted were drowsiness, anorexia, unsteadiness, and headaches; such symptoms usually resolved after the first 3 weeks of treatment. In only 2 instances was it necessary to discontinue treatment because of intolerance. *Fergus R. Ferguson*

201. **Primidone in Mental Deficiency Practice**
D. S. SHARPE. *British Medical Journal* [*Brit. med. J.*] **2**, 627–629, Sept. 11, 1954. 5 refs.

The efficacy of primidone (" mysoline "; 5-ethyl-5-phenyl-hexahydropyrimidine-4:6-dione) in controlling attacks in 38 mentally defective patients with grand-mal epilepsy was studied at Botleys Park Hospital, Chertsey, Surrey. Some of these patients had accompanying petit mal. Ages ranged from 7 to 52 years. In addition to assessing the results of treatment in major epilepsy, particular attention was paid to the changes, both clinical and electroencephalographic, in the patients with petit mal, and to the correlation between the initial intelligence quotient (I.Q.) and age of the patient and the results obtained. The daily dose of primidone was usually 1 g., although up to 2 g. was used in certain cases.

Of the 38 patients, 14 responded to treatment, the frequency of the attacks falling by 20% or more; 2 became completely free from attacks. Of the remainder, 8 derived no benefit from the drug and 11 became worse. In 3 administration of the drug was discontinued. Behaviour disturbances became more prominent in the 10 children treated and in one adult; the behaviour of the remaining adults was not affected. The fact that the best results were obtained in patients whose initial I.Q. was above 25 led the author to conclude that patients of low I.Q. are less likely to respond favourably to treatment. The age of the patient did not appear to affect the results.

In confirmation of the finding of other authors primidone proved to be relatively free from serious toxic effects. *Fergus R. Ferguson*

202. **Megaloblastic Anaemia Due to Phenytoin Sodium**
C. F. HAWKINS and M. J. MEYNELL. *Lancet* [*Lancet*] **2**, 737–738, Oct. 9, 1954. 7 refs.

203. **" Rotational " Epilepsy.** (Ротаторный вариант эпилептического припадка)
V. V. MIKHEEV and A. KH. SHTREMEL'. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 553–558, July, 1954. 20 refs.

Writing from the epilepsy clinic of the Bekhterev Institute, Leningrad, the authors review the literature on " rotational " epilepsy and report the further case of a youth aged 17 in whom rotational epileptic fits had begun suddenly at the age of 9. These were characterized by a convulsive turning of the head to the left, followed by a leftward rotation of the entire body if the patient was upright. Before the onset of the fits the boy had been of normal intelligence, but this gradually deteriorated as

the fits occurred more frequently and later assumed the character of grand mal. Analysis of the clinical and laboratory findings suggested that in this case there was a diffuse cerebral abnormality, with focal manifestations localized to the right frontal lobe. *L. Crome*

204. **The Detoxicating Function of the Liver in Epilepsy.** (Об антитоксической функции печени при эпилепсии)
T. S. ZAICHKINA. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 549–550 July, 1954.

The author has studied the hippuric acid excretion of 38 patients with epilepsy of varied aetiology seen at the Institute of Psychiatry, Moscow. After the administration of sodium benzoate the excretion of hippuric acid was diminished in most of the patients, the mean level for the group being only 45% of normal. It is evident to the author that the disturbance in the detoxicating function of the liver revealed by this test plays a significant role in the production of fits, even if it is impossible to decide whether this disturbance is primary or secondary. *L. Crome*

205. **Water Excretion and Water Concentration by the Kidneys in Epilepsy.** (О водовыделительной и концентрационной функции почек при эпилепсии)
N. S. IVANOVA. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **54**, 551–552, July, 1954.

Tests of renal function carried out on 26 epileptic patients showed that water excretion after the administration of 1,500 ml. of water was normal in 4 cases, below normal in 19, and above normal in 3. Urine concentration was abnormal in all 26 cases. These deviations from normal renal function are regarded as being possibly secondary to the convulsive phenomena. *L. Crome*

SPINAL CORD

206. **Spinal Cord Compression Studies. IV. Outlook with Complete Paralysis in Man**
I. M. TARLOV and E. HERZ. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **72**, 43–59, July, 1954. 1 fig., 17 refs.

After reviewing the literature the authors present a careful analysis of 72 cases of complete spinal paralysis which was undertaken in order to provide the evidence necessary to determine whether or not to operate, and if so when, on patients with this lesion. The 72 cases were composed as follows: (*a*) 35 cases of complete spinal paralysis of traumatic origin, 9 of which were not operated on and served as controls; (*b*) 27 cases of complete paralysis due to an extradural spinal tumour, of which 6 were not surgically explored; and (*c*) 10 cases of intradural spinal benign encapsulated tumour in which there was complete paralysis.

The authors conclude that the outlook as regards recovery of function is poor after the acute onset of complete sensori-motor loss due to a spinal-cord lesion, except for the rare cases of spinal-cord concussion. When, however, there is any evidence of spinal-cord conduction, either sensory or motor, through the area of the lesion, considerable or even complete restoration of function may occur. They further conclude that operation in cases of acute complete traumatic paraplegia may be of benefit only if performed within an hour or so of the accident; the more acute the onset of paralysis, the more urgent an attempt to alleviate the condition of the compressed spinal cord becomes.

G. S. Crockett

207. **The Problem of Evaluating Treatment of Protruded Lumbar Intervertebral Disk. Observations of Results of Conservative and Surgical Treatment in 429 Cases**
C. H. MILLIKAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 1141–1143, July 24, 1954. 2 refs.

The follow-up results in 429 cases of protrusion of a lumbar intervertebral disk, 329 of which were treated surgically and 100 conservatively, are reviewed in this paper from the State University of Iowa. Conservative treatment consisted in rest in bed for 10 to 14 days and application of heat and massage, followed by restricted physical activity. Surgical treatment consisted in exploration, removal of a considerable amount of disk substance, and, in 49 cases, spinal fusion. Discussing the indications for surgery, the author states that between 1939 and 1947 a total of 349 cases were operated on (including the 329 followed up) and in 23 (6·6%) of these no disk lesion was found. Of these 23 patients, 10 had no pain below the knee, 20 had no lumbar-spine stiffness, and in 21 the ankle-jerks were equal. The author suggests that caution should be exercised in advising surgical treatment in such cases.

The results were assessed 3 or more years after treatment from the replies to a questionary and, in some cases, re-examination as well. Satisfactory relief of pain in the back and leg was noted by 78% of the patients treated conservatively and by 83% of those operated on. The numbers in each group who were able to return to their former work or had a working capacity of 75% or more were about equal. In three respects, however, there was a significant difference between the two groups: (1) half of the patients operated on were able to return to their former work at 100% capacity, compared with only 30% of those treated conservatively; (2) there was a recurrence of the attack in only 5% of those treated surgically, while 60% of the conservatively-treated group had a recurrence; (3) subsequent operation was necessary in 2·8% of patients operated on as against 10% of the patients treated by conservative measures. Thus when the results in the two groups are compared, it would appear that patients operated on not only have a slightly better chance of obtaining relief from low back pain and from leg pain and a considerably better chance of achieving 100% working capacity in their former occupation, but they are also almost immune from recurrent attacks.

[Assuming that the two groups are comparable, surgical treatment appears to have been much more effective than the conservative treatment outlined.]

Brodie Hughes

Psychiatry

208. **A Comparative Study of Results in Neurotic Patients Treated by Two Different Methods**
A. HARRIS. *Journal of Mental Science* [*J. ment. Sci.*] **100**, 718–721, July, 1954. 3 refs.

The author describes an investigation of the comparative efficacy in psychoneurotic patients of Meduna's carbon dioxide method of treatment and psychotherapy on analytical lines, consisting of individual or group sessions, or both, conducted under expert supervision. A total of 120 neurotic patients attending the outpatient department of the Maudsley Hospital, London, were divided into two groups which were very similar as regards age and sex distribution and marital state of the patients, diagnosis, severity of the illness, and duration of symptoms. In each group there were 22 patients who either did not receive treatment for various reasons or had to be admitted to hospital.

The remaining 38 patients in each group were subjected respectively to the carbon dioxide method of treatment and psychotherapy. The patients were reexamined 12 to 15 months after they first attended the clinic, and their response to treatment was assessed by means of social criteria of a fairly objective kind. Analysis of the results did not reveal any significant difference between the two groups, but psychotherapy was more frequently considered helpful by the patients, even if they had not benefited from it objectively.

F. K. Taylor

209. **Carbon Dioxide Therapy of the Neuroses**
D. H. CLARK. *Journal of Mental Science* [*J. ment. Sci.*] **100**, 722–726, July, 1954. 11 refs.

The results obtained by strict application of Meduna's carbon dioxide method in the treatment of 42 psychoneurotic patients attending the Maudsley Hospital, London, are reported. Of these, 20 were improved, 13 were unchanged, and 9 became worse. However, only 24 patients received a course of more than 10 applications; the remainder gave up treatment prematurely. Patients suffering from obsession did not benefit.

In the author's view the treatment is physically safe, but must be carefully controlled since it may lead to psychotic breakdown. *F. K. Taylor*

210. **Clinical Signs, Diagnosis and Prognosis in the Functional Psychoses**
A. HARRIS and V. NORRIS. *Journal of Mental Science* [*J. ment. Sci.*] **100**, 727–731, July, 1954. 9 refs.

A group of 187 patients suffering from functional psychoses who were first admitted to a mental hospital before the age of 40 were followed up for 10 years, the object being to ascertain the prognostic value of simple clinical signs. The prognosis was assessed according to the length of stay in hospital during the follow-up period.

The patient's affective state was found to be of greatest prognostic significance. The outcome was favourable in 77% of the patients with consistent depression or elation, but in only 21% of those with shallow or inappropriate affect. Thought disturbances, hallucinations, and delusions did not by themselves affect the prognosis.

F. K. Taylor

211. **A Possible Relationship between Psychological Factors and Human Cancer**
E. M. BLUMBERG, P. M. WEST, and F. W. ELLIS. *Psychosomatic Medicine* [*Psychosom. Med.*] **16**, 277–286, July–Aug., 1954. 3 figs., 18 refs.

At the Veterans Administration Hospital, Long Beach, California, two groups, each of 25 patients with cancer and of similar age range and intelligence level, were given a personality test, the Minnesota Multiphasic Personality Inventory. This test is self-administered, machine-scored, and reasonably objective. The tests were carried out while the patients were in a phase of remission. Group 1 consisted of patients with rapidly progressing, uncontrollable disease, and Group 2 of patients with slowly progressing, easily controllable disease.

The two groups were easily distinguishable by the test results, the correct category being predicted from the record in 39 of the 50 cases, an accuracy of 78%. The possibility of this occurring by chance is less than 1 in 100. Most of the cancer-resistant patients (Group 2) seemed able to avoid or reduce excessive emotional tension by one of several defence mechanisms, an ability which was lacking in those in Group 1. The authors discuss the possible significance of these findings in relation to host resistance and believe that this study may help in answering the problem why some patients succumb more readily to cancer than others.

Desmond O'Neill

212. **Clinical Studies of Lysergic Acid Diethylamide.** [In English]
E. W. ANDERSON and K. RAWNSLEY. *Monatsschrift für Psychiatrie und Neurologie* [*Mschr. Psychiat. Neurol.*] **128**, 38–55, July–Aug., 1954. 13 refs.

The effects of D-lysergic acid diethylamide (L.S.D.) were studied in 4 normal subjects and 19 patients, 5 of whom were suffering from anankastic disorder, 4 from hysteria (including one case of psychogenic amnesia), 3 from sensitive paranoid reaction, 5 from schizophrenia, and 2 from endogenous depression, their ages ranging from 21 to 49 years. The drug was administered by mouth to the fasting subject on 58 separate occasions in doses ranging from 10 to 600 μg. The subjects were under continuous psychiatric supervision during the period of acute intoxication, the patients being confined to bed. The observation room was not darkened. Symptoms of intoxication appeared 15 to 60 minutes,

and the maximum effect 105 to 230 minutes, after administration. The authors present their own findings and relate them to those of other workers.

Visual disturbances of various kinds occurred in 15 subjects, and auditory phenomena in 8. Cutaneous sensation was modified in 8 subjects, paraesthesiae of the face being common, and taste was affected in 6 subjects, a "metallic" taste and "unpleasant" flavour being reported. Space perception was disturbed in 13 cases, 10 subjects having a sense of spatial insularity in which their immediate environment seemed to be entirely detached from its wider setting. Thought disorder was noted by 16 subjects, a tendency for thoughts to vanish suddenly being the commonest, while difficulty in concentration, impairment of grasp, and reduction of problem-solving performance were also frequent. Intensification or change of mood was very common (23 subjects), a tendency to spontaneous marked fluctuations being a striking feature in some cases. Anxiety, usually transient, occurred in 12 subjects at some stage, but euphoria and elation were commoner than depression. Sexual excitement was provoked in 7 females and one male and paranoid attitudes were accentuated or developed in 8 cases.

A disturbance of ego-experience occurred in 15 subjects, in 7 of whom there was a feeling of impending ego-dissolution, usually accompanied by considerable anxiety; this was not necessarily associated with higher doses. Depersonalization occurred in 6 subjects, sometimes as a transient state, and time disorders in 13. Change in body image occurred in 11 subjects, the most frequent being a curious feeling of lightness, so pronounced at times as to create a sensation of floating; a feeling of general diminution in size of the body or increase in size of a part of the body also occurred. Symptoms attributable to autonomic disturbance were noted by 18 subjects, nausea, dizziness, and a feeling of warmth being the commonest. Drowsiness occurred in 8 subjects. In 5 of 8 subjects a slight increase in the alpha-rhythm frequency of between 0·5 and 2 c.p.s. was noted in the electroencephalogram during intoxication. Glucose tolerance was found to be slightly diminished in tests performed on 6 subjects during 9 administrations. In 6 patients the change in the clinical picture following L.S.D. outlasted the period of intoxication. Large single doses (450 to 600 μg.) resulted in the development of a very labile state in which mood fluctuated between aggressive euphoria and agitated depression, with transient auditory hallucination, body-image disturbances, and time disturbance.

The results of these experiments confirm the findings of most previous authors that L.S.D. is a highly active substance producing in very small dosage psychological disturbances of type familiar in acute toxic states, though not involving any considerable clouding of consciousness. The authors, however, noted certain phenomena which have not previously been emphasized—the sexual excitement, which occurred in rather more than one-third of their cases, the sudden and striking changes of mood, the alarming sensation of impending ego-dissolution, and the variable effect of L.S.D. on the same subject from day to day. *John C. Kenna*

213. **Isoniazid Treatment of Psychiatric Patients**

F. LEMERE. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **71**, 624–625, May, 1954. 4 refs.

Of 65 psychiatric patients treated with isoniazid, only 8 showed any improvement that seemed to be definitely related to the drug or its suggestive effect. The effect of isoniazid on the personality is varied and unpredictable, but in general it appears to be that of a stimulant in smaller doses and of a neurotoxin in larger doses. Isoniazid is of very limited, if any, value in the treatment of psychiatric patients. It occasionally seems to help overcome fatigue, mental sluggishness, or depression associated with any of the various reaction types. —[Author's summary.]

214. **The Use and Action of Chlorpromazine in Psychoneuroses**

G. GARMANY, A. R. MAY, and A. FOLKSON. *British Medical Journal* [*Brit. med. J.*] **2**, 439–441, Aug. 21, 1954. 3 refs.

The effect of chlorpromazine in the treatment of 29 psychoneurotic patients at Westminster Hospital, London, is described. After an initial trial, the drug was given by mouth in a dosage of 25 mg. three times a day, rising by 25 mg. on alternate days to 75 mg. three times a day when necessary. The duration of treatment varied from 4 weeks to 4 months, maximum improvement being observed after 4 to 6 weeks.

Of 4 patients with mainly hysterical symptoms, 2 showed improvement and 2 only slight relief of tension; of 6 with phobia as the chief feature, one did not improve, 4 had some relief of tension, and one had considerable relief; of 3 patients suffering mainly from depression, 2 showed no improvement, while one had slight relief of tension; of 5 with mainly obsessional symptoms, 2 experienced slight relief of tension, 3 moderate relief, and one marked relief; no relief was obtained by 2 patients with non-psychogenic pain; of 6 patients suffering from moderate to severe tension, 2 experienced relief and 4 complete or marked relief; finally, all of 3 patients with dysmenorrhoea obtained considerable relief. A clinical assessment of the response of each patient "as a whole unit" showed that 10 were much improved, requiring no further treatment other than chlorpromazine at periodic brief interviews. All the patients with tension as the predominant symptom improved; however, no case of agitation, as opposed to tension, was included in the series.

Complications included tachycardia with dryness of the mouth; transient weakness of the legs; tachycardia with a fall in blood pressure of over 40 mm. Hg (2 cases of hypertension); a rise in temperature to 103° F. (39·4° C.) after 7 to 10 days' treatment, accompanied by perspiration, nausea, epigastric discomfort, and tenderness; and abnormal "bromsulphalein" retention with bile salts in the urine.

The authors state that the results in this series have not confirmed the value claimed for the drug in the treatment of "psychasthenic" illness, but that its value in the treatment of tension states appears to have been adequately established. *G. de M. Rudolf*

Dermatology

215. Prolonged Therapy with Cortisone for Chronic Skin Diseases

M. B. SULZBERGER and V. H. WITTEN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 954–959, July 10, 1954. 2 figs., 7 refs.

The dermatological indications for cortisone therapy can be divided broadly into two groups: (1) as a short-term measure in certain acute but ordinarily self-limited eruptions, such as widespread eczematous dermatitis, acute urticaria, angioneurotic oedema, and certain drug reactions; and (2) for long-term use in (*a*) certain chronic, not ordinarily fatal, but severely incapacitating dermatoses, such as atopic dermatitis, exfoliative erythrodermia, and exudative discoid and lichenoid chronic dermatosis, and (*b*) ordinarily fatal but chronic conditions such as pemphigus and acute disseminated lupus erythematosus. When cortisone has to be given daily in doses of 75 mg. or more for months or even years special problems arise and the authors discuss these on the basis of some 4 years' experience. They first emphasize the need before treatment to exclude the presence or history of cardiac, renal, or pulmonary disease, gastric or duodenal ulcer, tuberculosis, diabetes, thromboembolic diseases, and psychiatric disturbances. This is always desirable even when short-term administration only is contemplated, and is imperative whenever a patient is expected to have to take cortisone for a prolonged period.

The results of the treatment with cortisone of 35 patients with a variety of dermatoses (including 15 cases of atopic dermatitis) for periods ranging from 2 months to several years are given in tabular form, and were almost universally good. The initial dosage varied from 300 to 1,000 mg. daily in the "fatal" conditions, whereas many of the non-fatal skin diseases could be brought under control by doses of 100 to 300 mg. a day. Otherwise healthy persons were given an initial dosage sufficiently large to allay the signs and symptoms rapidly, the dosage then being reduced as rapidly as possible to the lowest effective maintenance level. In general it was found inadvisable to attempt to relieve the signs and symptoms completely, adverse effects being better avoided by giving doses just short of the amount required to achieve this. Such adverse reactions rarely occurred except when doses of more than 100 to 125 mg. were given daily for a protracted period. As precautionary measures the blood pressure and weight were recorded frequently, the urine tested for sugar, and a salt-poor diet given together with a daily supplement of 3 g. of potassium chloride in several doses.

The authors stress the need for the regular and frequent supervision of ambulatory patients and emphasize that cortisone may mask the signs of active infection, render painless the perforation of a viscus, reduce fever, and maintain a feeling of well-being in the face of serious infection and destruction of tissue. Their most encouraging experience in the prolonged administration of cortisone was that in almost all cases they were able to reduce the dosage, often to merely a fraction of that originally required, and in a few cases to discontinue the hormone altogether without a recurrence of the disease. There were no instances of acquired drug resistance or of addiction. *E. W. Prosser Thomas*

216. The Melkersson–Rosenthal Syndrome. (Le syndrome de Melkersson–Rosenthal)

J. PIÉRARD and J. MAGE. *Archives belges de dermatologie et de syphiligraphie* [*Arch. belges Derm. Syph.*] **10**, 1–25, May, 1954. 11 figs., 19 refs.

The Melkersson–Rosenthal syndrome is characterized by the following triad of signs: (1) recurrent facial paralysis; (2) oedema localized to the face, particularly the lips; and (3) a plicated or "scrotal" tongue. The disorder is said to begin in infancy or adolescence with a transitory peripheral facial paralysis, which may be accompanied by a non-inflammatory oedema of the face and lips, but more commonly the latter sign appears later, in some cases only after a number of years. Further attacks follow and the oedema may become permanent. Additional symptoms, such as migraine, mild auditory and vestibular disturbances, or hyperaesthesia in the region of the trigeminal nerve, may also occur. Sex distribution appears to be about equal; of 28 collected cases, 12 were in men and 16 in women.

In this paper the authors discuss the literature dealing with the symptomatology, pathology, aetiology, and treatment of the condition, and describe in detail a case seen by them at the Military Hospital, Brussels, in 1953. The patient was a man of 21 who complained of a swelling of the upper lip, which had begun suddenly 14 months previously and subsided, but had then recurred 6 weeks before admission to hospital. The first attack was preceded by a painful swelling of the tongue, and the patient also reported that he had had three attacks of localized facial paralysis each lasting 2 to 3 months when he was 6, 10, and 15 years of age. The patient's personal and family medical history revealed nothing significant; extensive clinical and laboratory investigations showed only some slight increase in pressure in the cerebrospinal fluid, which was otherwise normal, and electroencephalography suggested the presence of a focus of discharge in the left anterior area of the brain.

The appearance of the plicated tongue and swollen lips are shown in photographs, and the histological appearances in biopsy specimens are illustrated with photomicrographs which show the presence superficially of intense oedema, some vascular congestion, but only slight infiltration with lymphocytes and histiocytes. More deeply, however, there are lesions of an involutive

myositis which the authors attribute to the intensity of the oedema. A comparison is made between this condition and that of *cheilite granulomateuse* described by Miescher (*Dermatologica*, 1945, **91**, 57) which, it is concluded however, is a separate entity.

Benjamin Schwartz

217. **Haematogenous Contact Eczema.** (Über das hämatogene Kontaktekzem)
E. BINDER. *Archiv für Dermatologie und Syphilis* [*Arch. Derm. Syph.* (*Berl.*)] **198**, 1–22, 1954. Bibliography.

Haematogenous contact eczema is produced by the internal administration (by ingestion or parenterally) of an antigen, among the commonest of which are sulphonamides, procaine, and penicillin. In contrast to the purely exogenous eczema, systems other than the skin are commonly affected and thus the symptomatology is more varied. The speed with which the reactions occur depends on whether or not the patient has already been sensitized by previous internal or external contact with the antigen. In general, a rise in temperature occurs in 80% of cases within a few hours of administration of the antigen, and a moderate polymorphonuclear leucocytosis with relative lymphopenia and eosinopenia develops during the next few days. As the leucocytosis declines, so the eosinophil leucocytes increase in number, this being regarded as the most constant single feature. In about 50% of cases lymphocytosis, sometimes with peripheral lymphadenopathy, is found at this stage. Other symptoms are vomiting, headache, and neck rigidity due to acute hydrocephalus, and in severe cases, profound shock. Vasomotor phenomena and, rarely, asthma may trouble the patient for a short time. Diarrhoea, stomatitis, rhinitis, and conjunctivitis may occur as the result of a reaction in the mucous membranes analogous to that of the skin. Renal disturbances may be most serious and may lead to anuric uraemia, especially in cases of sensitization to iodine and mercury.

A short review of 33 personal cases is given. It was found that a negative reaction on patch testing with an antigen did not exclude sensitization, oral administration of the same antigen often giving a positive reaction.

G. W. Csonka

218. **Further Experience in the Treatment of Tuberculosis of the Skin with Isoniazid.** (Weitere Erfahrungen in der Behandlung von Hauttuberkulosen mit Isonikotinsäurehydrazid (Neoteben))
O. BRAUN-FALCO. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **130**, 719–729, 1954. Bibliography.

The author presents, from the Dermatological Clinic, University of Mainz, results of the treatment of 166 cases of cutaneous tuberculosis (of which 142 were cases of lupus vulgaris) with isoniazid (" neoteben ") during the last 3 years. Clinically, healing usually began at once, but histologically, perivascular lymphocytic infiltration could be demonstrated in spite of apparent clinical cure; it is pointed out that theoretically recurrence may start from such a focus. The total dosage of isoniazid depended on the location and character of the lesions. Thus active forms of lupus vulgaris responded well to treatment, but a high dosage was sometimes required for a recurring lesion on a scarred area. There was, however, no relation between the size of the lesion and the dose required. The total dosage therefore varied from 10 to 100 g. (average about 32 g.) given over periods up to 3 months in daily doses of 4 or 5 mg. per kg. body weight; the author points out that these doses are rather smaller than those given by other workers.

In 4 cases the treatment had to be discontinued because of undesirable side-effects, 3 cases deteriorated during treatment, and 14 were not improved. Distinct improvement, however, was achieved in 119 cases. Some cases resistant to isoniazid alone responded well to a combination of the drug with vitamin D (" vigantol ") or with streptomycin. Where indicated, surgical treatment was carried out under the protection of isoniazid, and in some cases additional treatment with Finsen or Kromeyer irradiation was also given. The follow-up period did not exceed one year in most cases, but in that period recurrences had already occurred in 18% of the cases; the recurring lesion usually responded again to isoniazid, and additional vitamin D had rarely to be given. The author believes that treatment should be continued for 4 to 5 months once an asymptomatic clinical state has been reached.

In 3 cases of uncomplicated tuberculous cervical lymphadenitis a total amount of 40 g. of isoniazid failed to produce significant improvement; 2 cases complicated by a fistula responded better, and in these the additional local application of 5% isoniazid or 10% streptomycin proved useful.

The few cases of scrofuloderma responded well to isoniazid alone. One case of a primary tuberculous complex on the cheek of a child aged 5 healed well under treatment with 50 mg. of isoniazid twice daily to a total of 24 g. Four cases of Bazin's disease also responded well, but in a case of lupus pernio (Boeck's sarcoid) there was no improvement. In 2 cases in the series a transitory granulomatous lesion (histologically closely simulating granuloma annulare) developed in the vicinity of the site of lupus vulgaris during treatment with isoniazid.

Ferdinand Hillman

219. **Antibiotic and Sulfonamide *in vitro* Studies in Pustular Acne Vulgaris**
R. O. NOOJIN, L. S. OSMENT, and C. H. WINKLER. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **70**, 222–227, Aug., 1954. 6 refs.

It has been found clinically that decided improvement follows administration of a sulphonamide or an antibiotic in some cases of pustular acne. In the present paper from the Medical College of Alabama, Birmingham, Alabama, the authors discuss the value of sensitivity tests *in vitro* in deciding which of these therapeutic agents should be tried first.

Sensitivity tests by the paper-disk and the tube serial dilution techniques were carried out on organisms isolated from acne pustules. The results obtained with the simpler paper-disk method were comparable with those obtained with the more time-consuming tube serial dilution technique when the same drugs were tested

against identical strains of staphylococci. The predominant organism isolated was a haemolytic *Staphylococcus albus*, against which penicillin proved to be the most effective antibiotic, with oxytetracycline, chlortetracycline (aureomycin), and chloramphenicol next, in that order. In general, dihydrostreptomycin and the sulphonamides were of little value.

Each of 24 patients with pustular acne which had failed to respond to routine treatment was given the antibiotic most likely to be effective, as indicated by a preliminary test *in vitro*. Of these patients, 17 received penicillin by mouth in a dosage of 100,000 units three times a day, 2 received chlortetracycline, and 3 received oxytetracycline, the dosage of the last two drugs being 250 mg. three times a day; the remaining 2 patients were first given penicillin and then oxytetracycline. In 20 cases the pustular element of the eruption improved in 1 to 2 weeks and in a further case improvement was noted when the antibiotic therapy was changed; no improvement was observed in 3 cases. The follow-up period was 3 months or longer; in 21 patients the clinical response was satisfactory so long as the antibiotic was taken, but relapse occurred when the drug was discontinued.

The authors conclude that the paper-disk method of determining bacterial sensitivity to antibiotics " deserves consideration as a preliminary qualitative guide in the management of patients with unresponsive pustular acne vulgaris ". *Benjamin Schwartz*

220. ***Pityrosporum ovale* Types Cultured from Normal and Seborrheic Subjects**

H. J. SPOOR, E. F. TRAUB, and M. BELL. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **69**, 323–330, March, 1954. 5 figs., 12 refs.

The incidence in man of scalp infections with *Pityrosporum ovale* and the association of this group of organisms with seborrhoeic conditions were studied at New York Medical College. *P. ovale* was grown on culture media consisting of wort agar fortified with oleic acid (1·5%), sodium ethyl oxalacetate (0·5%), and aneurin (0·1%). This medium inhibited the growth of bacteria and mould contaminants, but lipophilic yeasts could grow in it. The cultures were incubated at 36° C. for 72 hours. Sampling was done by scraping the scalp with a sterile tooth-brush, which was then dropped into sterile distilled water. Cultures were plated out from the suspension of scrapings in distilled water. Four types of *P. ovale* were isolated, differing mainly in the colour of the colony, which was variously tan, white, black, and salmon pink. Morphologically, the cells of the four types were similar, most of them being 4 to 5 μ in diameter, although smaller and larger cells were seen; there were many bottle-shaped budding cells. The larger cells were apparently encapsulated in some gelatinous material. Extreme pleomorphism of the organism was observed when studied by direct mount.

Scrapings from the scalp of 196 men were examined, and *P. ovale* was found in 64·8%. Type 1 (light tan colour, smooth, moist, and glistening) was most frequently encountered. The incidence of *P. ovale* fell markedly in the age group 46 to 60, but rose again in patients over 60. No relationship was found between the presence of *P. ovale* and the incidence of seborrhoeic infection. *Kate Maunsell*

DERMATOSES

221. **Studies of Typical and Atypical Lichen Ruber Planus (Erosive, Haemorrhagic, Cicatricial, and Alopecic) in Relation to Changes in Protein Metabolism.** (Études sur le lichen ruber planus typique et atypique: ulcéro-érosif, ulcéro-hémorragique, scléro-cicatriciel, alopécique, et sur ses rapports avec les modifications de la protidopoïèse)

G. SANNICANDRO. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph.* (*Paris*)] **81**, 380–398, July–Aug., 1954. 13 figs., 17 refs.

A clinical and histological study of 8 cases of lichen planus, some of which presented unusual clinical signs, is presented. The author states that the well-known lymphohistiocytic infiltrate in the papillary layer of the dermis is not the only important change in this condition, other significant histological features being permanent damage to the pilar apparatus, infiltration with plasma cells and fibroblasts, and a peculiar hyaline sclerosis due to a disturbance of protein metabolism, accompanied by a variable increase in the gamma-globulin content of the blood. *James Marshall*

222. **Lupus Erythematosus. Treatment by Combined Use of Massive Amounts of Panthothenic Acid and Vitamin E**

A. L. WELSH. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph.* (*Chicago*)] **70**, 181–198, Aug., 1954. Bibliography.

The literature on the metabolic functions of pantothenic acid and vitamin E (α-tocopherol) is reviewed at length, and the results of the use of these compounds in the treatment of lupus erythematosus are summarized. The author believes that many of the failures have been due either to the fact that these vitamins were administered individually instead of in combination, or to inadequate dosage.

To 67 patients suffering from lupus erythematosus massive doses of pantothenic acid combined with α-tocopherol were given, the treatment schedule being 10 to 15 g. daily of calcium pantothenate, 10 to 15 g. daily of pantothenyl alcohol, and 5 to 10 g. daily of sodium pantothenate, combined with 3 to 6 g. daily of a mixture of three tocopherols. In a group of 36 patients with chronic discoid lupus erythematosus objective improvement was observed in 4 to 6 months; in half the patients the condition had cleared completely and in the remainder it was much improved at the time of reporting. Similar results were obtained in a group of 17 patients with disseminated discoid lupus erythematosus, improvement being noted after 2 months, and in 11 with the subacute disseminated form of the disease, the response in this group being rapid, usually after one month. In 3 cases of acute disseminated lupus erythematosus treatment was started while the acute phase was being brought under control with steroid hormones; by administration of

pantothenic acid and tocopherol the patients were maintained without relapse for 7, 11, and 19 months respectively. In general, it was noted that the more hypertrophic and infiltrated the process, the slower the response. Apart from transient nausea and gastric distress there were no complications, and there were no abnormal findings in the blood or urine of patients treated for 1 to 3 years.

Discussing the results, the author suggests that as α-tocopherol may be metabolized in the body to furnish precursor " cortisone-like materials ", and pantothenic acid is related to the secretion and formation of steroid hormones—a theory supported by the functional inadequacy of the adrenal cortex in pantothenate deficiency —massive dosage of pantothenic acid with α-tocopherol enables the body slowly to synthesize a cortisone-like compound. *Benjamin Schwartz*

223. **Nikolsky's Sign in Pemphigus Foliaceus.** (Note sur l'importance du signe de Nikolsky dans le pemphigus foliacé)
A. F. Martins de Castro and J. J. Angulo. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **81**, 399, July–Aug., 1954. 2 refs.

A total of 149 cases of pemphigus foliaceus were studied at the Butantan Institute, São Paulo, Brazil. In 8 cases in complete remission Nikolsky's sign was always absent. Of 29 cases in partial remission the sign was present in 7 and absent in 22. Of 112 cases in the chronic phase, the test gave a positive result in 93 and a negative result in 19. *James Marshall*

224. **Relationship between the Rate of Absorption of Saline Solutions Injected into the Dermis and Certain Clinical Phases of Pemphigus Foliaceus.** (Rapport entre le taux de résorption d'une solution saline injectée dans le derme et certaines phases cliniques du pemphigus foliacé)
J. J. Angulo and A. F. Martins de Castro. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **81**, 400–403, July–Aug., 1954. 19 refs.

From experiments carried out on 153 cases of pemphigus foliaceus at the Butantan Institute, São Paulo, Brazil [see Abstract 223], there appeared to be a definite relationship between the time of absorption of injected saline from the dermis and the phase of the disease, pathologically accelerated absorption being noted in 79% of chronic cases and in only 39% of cases in partial remission. *James Marshall*

225. **Pituitary and Adrenocortical Function in Pemphigus Foliaceus.** (Sur la fonction hypophyso-adréno-corticale dans le pemphigus foliacé)
J. J. Angulo and L. E. Ferraz-Mazzoni. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **81**, 404–408, July–Aug., 1954. 18 refs.

In 28 cases, 17 chronic and 11 in partial remission, of pemphigus foliaceus studied at the Butantan Institute, São Paulo, Brazil [see Abstracts 223 and 224], the degree of eosinopenia occurring after injection of adrenaline suggested the presence of hypophyso-adrenocortical dysfunction. The fasting eosinophil count was increased in these patients. In no case had the injection of adrenaline any effect on the urinary uric acid : creatinine ratio. *James Marshall*

TUMOURS

226. **Treatment of Plantar Warts with Carbon-dioxide Snow**
K. D. Crow and O. L. S. Scott. *Lancet* [*Lancet*] **2**, 312–314, Aug. 14, 1954. 1 fig., 1 ref.

Ideally, the treatment of plantar warts should be rapid, relatively painless, and easy to apply. The authors have re-examined the method, " long since fallen into disrepute ", of freezing with solidified carbon dioxide, and suggest that its unreliability may have been due to failure to remove the hyperkeratotic cap of the wart before freezing.

In the method adopted at St. Thomas's and three other hospitals in or near London, the warts to be treated were pared down with a scalpel till bleeding points of papillae were exposed. The wart was then frozen with a stick of carbon dioxide snow for 5 minutes. After a week the roof of the blister was removed along with the wart and a dressing applied to the underlying raw surface. In a series of 200 unselected cases thus treated the cure rate was 93%, compared with 81% in a similar group of 67 cases treated by curettage and cauterization. The rate of recurrence within 6 months in the two groups was 7% and 19% respectively. Contrary to a generally held impression, the authors found that freezing for periods up to 5 or 6 minutes caused no more discomfort than freezing for much shorter periods.
John T. Ingram

227. **A Contribution to the Clinical and Histological Study of Morphoea-like Epithelioma.** (Contribution à l'étude clinique et histologique de l'épithélioma morphéiforme)
S. Lapière and J. Piérard. *Annales de dermatologie et de syphiligraphie* [*Ann. Derm. Syph. (Paris)*] **81**, 365–379, July–Aug., 1954. 9 figs., 29 refs.

Morphoea-like epithelioma is a variety of basal-cell carcinoma and has to be distinguished clinically from cicatricial and " pagetoid " basal-cell carcinomata, morphoea, and *hypodermites sclérodermiformes* (Gougerot). The tumours have a marked tendency to infiltrate, but remain below the epidermis, which is not elevated and very rarely ulcerated. The tumour cells run generally in narrow, tortuous, ramifying columns or in larger clumps with ragged convoluted edges. Cellular elements are of basal-cell type. The epitheliomatous tissue may show signs of differentiation towards glandular or pilar structures. Narrow columns of cells are isolated by a fibrous or sclerous stroma, while larger clumps of cells are surrounded by a collagen layer isolating them from the fibrous stroma.

The tumour arises from the basal layer of the epidermis, hair follicles, or sweat glands, and its origin is often multicentric. *James Marshall*

Paediatrics

228. **A Study of Early and Later Introduction of Solids into the Infant Diet**
R. W. DEISHER and S. S. GOERS. *Journal of Pediatrics* [*J. Pediat.*] **45**, 191–199, Aug., 1954. 2 figs., 3 refs.

A study was made of the progress of 85 infants from a homogeneous background divided into two groups designated as early and later feeding. Infants in both groups were either breast fed or given formulas plus multivitamins and orange juice from birth. Solids were introduced in the early feeding group during the first 4 weeks of life and in the later feeding group during the ninth to twelfth week age period.

Four hundred and nineteen hemoglobin and red blood cell determinations were made on the blood samples of 45 infants in the early feeding group and 382 hemoglobin and red blood cell determinations were made on the blood samples of 40 infants in the later feeding group. The *t* test of significance applied to the mean hemoglobin and red blood cell determinations for the months of greatest deviation between the two groups reveals no significant difference. After the third month the mean hemoglobin value was around 11 g. per 100 ml.

Growth between the two groups was comparable, as was the number of illnesses, character of the stools, number of stools, incidence of diarrhea, constipation, colic, excessive regurgitation, and number of food refusals.—[Authors' summary.]

NEONATAL DISORDERS AND PREMATURITY

229. **Spontaneous Regression in Retrolental Fibroplasia**
W. C. OWENS. *Transactions of the American Ophthalmological Society* [*Trans. Amer. ophthal. Soc.*] **51**, 555–579, 1953 (published 1954). 9 figs., 35 refs.

The author reviews the clinical course and pathology of retrolental fibroplasia, and points out that the tendency of the disease to undergo spontaneous regression has generally not been fully appreciated. At the Harriet Lane Home of the Johns Hopkins Hospital, Baltimore, 128 premature infants weighing less than 3 lb. (1,360 g.) at birth were observed. In 32 (44%) of the 73 in whom some manifestation of acute retrolental fibroplasia was present in one or both eyes, no residual changes were visible after the acute stage had regressed; in a further 22 (30%) the residual changes were of a minor nature, such as distortion of the disk or retinal folds; while in only 19 (26%) of the infants affected did a partial or complete retrolental membrane form. The extent of involvement during the acute phase is described.

The author classifies the residual manifestations in five grades: (1) minor manifestations which may be no more than a moderate or high degree of residual myopia, or small areas of retinal atrophy often associated with pigmentation; (2) distortions of the disk and retinal vessels; (3) retinal folds extending from the disk to a mass of scar tissue at the periphery; (4) retinal detachment, with a mass of tissue filling one sector or the circumference of the retrolental space; a good red reflex can be obtained through the remaining portion, and in such cases distortions of the disk or areas of pigmented scarring can be seen; (5) detachment of the entire retina, with the formation of a mass of disorganized tissue completely filling the retrolental space.

J. R. Hudson

230. **Pathological Basis of Retrolental Fibroplasia**
N. ASHTON. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **38**, 385–396, July, 1954. 14 figs., 19 refs.

The development of retrolental fibroplasia may be described as occurring in three stages: (1) proliferation of vaso-formative tissue in the inner layers of the retina and its extension into the vitreous; (2) commencing retinal detachment with formation of fibro-vascular bands in the vitreous; and (3) total retinal detachment and formation of a dense retrolental membrane.

In this paper detailed pathological findings in 4 cases representative of the early stages are recorded. Retrolental fibroplasia has not been seen in any stillborn or premature infant dying soon after birth. It is suggested that some of the cases which have been reported as of prenatal origin because of the presence of areas of proliferation in the retina may have shown the normal appearances of endothelial and mesenchymal proliferation associated with normal vascular development of the retina. There may be causes other than oxygen administration which would produce the same pathological changes, and it is suggested that a special name should be given to the oxygen-induced disease.

D. A. Langley

231. **Effect of Oxygen on Developing Retinal Vessels with Particular Reference to the Problem of Retrolental Fibroplasia**
N. ASHTON, B. WARD, and G. SERPELL. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **38**, 397–432, July, 1954. 30 figs., 52 refs.

The degree of retinal vascularization in the full-term kitten at birth is very similar to that of the premature infant, and for this reason kittens were used at the Institute of Ophthalmology, London, in an investigation of the effects of high oxygen concentration on the developing retinal vessels. Exposure of the animal to a high concentration of oxygen produced obliteration of the retinal vessels, the severity of this effect being inversely proportional to the degree of maturity of the vessels and directly proportional to the duration of exposure and to the concentration of oxygen. Concentrations below 35% had little or no effect in the most sensitive age groups, nor did higher concentrations when the

vessels were more mature. On transfer of the kittens from a high-oxygen atmosphere to air, the obliterated vessels reopened only partially owing to thrombosis or adherence of the vascular walls. The retina was revascularized by profuse and disordered proliferation of vessels which invaded the vitreous, producing a picture similar to that of the first stage of human retrolental fibroplasia. Retinal detachment did not occur in the kitten. "Tromexan" (ethyl biscoumacetate) administered before and during the experiment lessened the vaso-obliterative effect, probably by reducing intravascular coagulation. A return to a high concentration of oxygen controlled to some extent this vasoproliferation, but subsequent removal to air again resulted in an exacerbation of the process.

The possible mechanisms are discussed and it is concluded that the high oxygen tension in the choroidal circulation removes the normal stimulus to retinal vascular growth, and that on removal to air this factor accumulates and stimulates vascularization to an excessive degree. An urgent plea is made for the control of oxygen therapy in the management of the premature infant. *D. A. Langley*

232. **Direct Observation of the Effect of Oxygen on Developing Vessels. Preliminary Report**
N. Ashton and C. Cook. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **38**, 433–440, July, 1954. 8 figs., 4 refs.

It was found in further experiments carried out at the Institute of Ophthalmology, London, that a high oxygen environment had no effect on the alloxan-produced vascularization of the rabbit cornea. Similarly, no alteration in the vascularization of a "perspex" chamber inserted into the rabbit's ear was observed.

The retinal vessels of the kitten were observed and photographed while the animal was exposed to air and to a high oxygen concentration. The cornea, anterior lens capsule, lens, and iris were removed and a perspex window fixed at the limbus by a metal ring. It was found that oxygen had no effect on the retinal vessels of the adult cat. In the kitten, vasoconstriction and capillary obliteration developed after 5 minutes' exposure to oxygen. The vessels reopened after about 10 minutes and remained in this state for about 5½ hours, when the delayed effects were seen. The vessels again constricted and total obliteration developed, becoming complete in about 8 hours. The circulation may be re-opened and closed again by alternating air and oxygen.
D. A. Langley

233. **Cyanosis from Absorption of Marking-ink in Newborn Babies**
I. F. MacMath and J. Apley. *Lancet* [*Lancet*] **2**, 895–896, Oct. 30, 1954. 6 refs.

234. **Iron Absorption in Premature and Full-term Infants**
L. Oettinger, W. B. Mills, and P. F. Hahn. *Journal of Pediatrics* [*J. Pediat.*] **45**, 302–306, Sept., 1954. 3 figs., 17 refs.

CLINICAL PAEDIATRICS

235. **Acute Infectious Lymphocytosis. Reports of an Outbreak**
H. E. Scalettar, J. E. Maisel, and M. Bramson. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **88**, 15–24, July, 1954. 3 figs., 27 refs.

Acute infectious lymphocytosis having been diagnosed in a boy with meningeal symptoms admitted to Kings County Hospital, Brooklyn, New York, from an institution, the authors performed blood counts on all the other inmates, those sleeping in the same dormitory as the patient being examined repeatedly. As a result they found 9 further acute cases and 7 cases which were thought to be in the convalescent stage. All these children had a mild upper respiratory infection, and 7 had diarrhoea. The leucocyte count was as high as 122,000 per c.mm., the great majority of the cells being lymphocytes. The average duration of leucocytosis was 30 days. Attempts to isolate a virus gave inconclusive results.

[The paper includes a useful review of the literature.]
R. S. Illingworth

236. **Acute Appendicitis in Childhood**
F. D. Hindmarsh. *British Medical Journal* [*Brit. med. J.*] **2**, 388–391, Aug. 14, 1954. 5 figs., 9 refs.

A series of 118 cases of acute appendicitis in children up to the age of 12 years which came under the author's care at the Royal Victoria Infirmary, Newcastle upon Tyne, are reviewed. In 63 cases localized or generalized peritonitis was present on admission, and in this connexion the author remarks that "any factor which may lead to delay in admission of over 24 hours is worthy of close study". Factors which may mislead the clinician and delay admission are vomiting as an initial symptom preceding the pain, and localized tenderness at other than the classic sub-caecal site. The condition should be diagnosed before rigidity develops. A graph shows the stage of development of the disease in relation to the day of admission. Most cases in which peritonitis was absent or localized were admitted during the first 3 days; those in which there was an abscess were commonly admitted from the second to the fifth days, while most of those with generalized peritonitis were admitted between the third and fifth days.

The importance in seriously ill patients of delaying operation until dehydration is corrected is stressed. Antibiotics were not given unless peritonitis was present; in cases of localized peritonitis penicillin and streptomycin were administered for 5 to 7 days, and in cases of generalized peritonitis aureomycin was given intravenously for 10 days. A muscle-splitting incision was used on 57 occasions, the Rutherford Morison muscle-cutting incision on 43, and the paramedian incision on 16. The appendix was removed at the initial operation in 110 cases and at a delayed operation (after 2 months) in 8. Abscess occurred in 24 cases; in 16 of these the appendix was removed at the time of drainage and in 6 drainage only was carried out, the remaining 2 cases

being treated conservatively. There was one death in the series. Complications were a subdiaphragmatic abscess in 2 cases and residual abdominal abscess in 9.

M. A. Birnstingl

237. **Non-specific Oesophagitis in Infants and Young Children.** (Über die unspezifische Oesophagitis bei Säuglingen und Kleinkindern)

A. ANGULO. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*) **65**, 193–203, 1954. 6 figs., 22 refs.

The author has examined, at the University Pathological Institute, Frankfurt am Main, the oesophagus in 100 children and infants, including 10 stillborn babies. No inflammatory changes were found in the 10 stillborn infants; all the cases (32) of oesophagitis were seen in subjects in the age group one day to 5 years, none being found among the 4 children examined aged 5 to 14 years. The highest incidence was among premature infants (10 cases) and children with cerebral diseases such as meningitis and encephalitis (11 cases). The author differentiates the following forms of oesophagitis: (1) acute or chronic oesophagitis with intact epithelium; (2) acute erosive oesophagitis; (3) superficial necrotizing oesophagitis; (4) pseudomembranaceous oesophagitis; and (5) phlegmonous oesophagitis. The histological findings are described, but do not differ from those reported previously by other workers. The author believes that circulatory disturbances in the vessels of the oesophageal wall are mainly responsible for the oesophagitis [although 20 (64%) of the patients with oesophagitis had vomited].

[No bacteriological findings are given nor any attempt made to correlate such with the type of inflammation. At a meeting of the Association of Clinical Pathologists in September, 1954, Lodge presented anatomical and experimental evidence which strongly suggested that reflux of acid gastric contents aggravated by the horizontal posture is the principal factor in the aetiology of non-specific oesophagitis.] *H. S. Baar*

238. **Alcoholism in Children.** (L'alcoolisme des enfants)

—. SERIN. *Bulletin de l'Académie nationale de médecine* [*Bull. Acad. nat. Méd. (Paris)*] **138**, 324–327, June 22, 1954.

Moodiness, behaviour disorders, insomnia, and nightmares are not uncommon symptoms in childhood, and even where the parents are alcoholic such symptoms are more likely to be attributed to the consequent environmental disturbances than to direct intoxication of the child itself. In a series of cases of disordered behaviour of obscure origin in children the author found that chronic alcoholic intoxication was in fact the cause and had been induced not through parental depravity, but through their ignorance of the undesirability of giving alcoholic drinks to young children. The discovery of such ignorance among Parisian parents in the higher social and cultural levels prompted an investigation into the habitual consumption of alcohol by children in all parts of France, a questionary being sent to all Departmental Directors of Health Services. The replies, although as yet incomplete, indicate an alarming state of affairs. The consumption of wine by school children with their midday meal is a common practice and in one Department it was estimated at half a litre per child per day. In at least one instance dilution of the wine was commonly condemned on the grounds that water was a possible medium of transmission of poliomyelitis and other diseases. Moreover, alcoholic beverages are used medicinally in many districts and at all social levels. Anisette has a reputation as a vermifuge, and brandy as a restorative after any of the minor physical or emotional crises of childhood. Together with various aperitifs and fortified wines they are frequently administered to the youngest of children by well-meaning if misguided parents.

The author (whose views were supported by several subsequent speakers) maintains that alcoholism in children is a real problem in France today. It is important not only because of its immediate effects in childhood, but also because it must often lay the foundations for chronic alcoholism in later life. She makes a strong plea for a national campaign of propaganda against this insidious danger, emphasizing that it is due to ignorance and custom and not to deliberate parental vice.

T. A. A. Hunter

239. **Disturbances of Sensation in Children with Hemiplegia**

J. P. M. TIZARD, R. S. PAINE, and B. CROTHERS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 628–632, June 12, 1954. 2 figs., 5 refs.

The authors draw attention to the presence and significance of sensory dysfunction in children with hemiplegia. A series of 106 such patients were subjected to sensory tests, including tests of vision and hearing, special attention being given to the cortical discriminatory functions such as stereognosis and two-point discrimination. These last two could be satisfactorily tested, as a rule, in intelligent children from the age of 5 years onwards. Impairment of sensation was found in about 50% of the patients, both among those with congenital hemiplegia and those with hemiplegia acquired later in childhood, although the number was slightly higher in the latter group. Hemianopia occurred rather less frequently, in about 25% of cases, and was rarely present without concomitant sensory impairment. Stereognosis was the function most often impaired alone; other types of sensation were not affected in the absence of astereognosis and loss of two-point discrimination.

The severity of the sensory involvement was not correlated with the severity of the motor disability; in fact impaired sensation was often itself the major reason for disuse of the arm. There was no correlation between the sensory disabilities and age at onset of the hemiplegia, mental status, or the occurrence of seizures, but close correlation was observed with under-development of the arm. The authors emphasize the importance of searching for sensory impairment, if necessary by re-examination of the child when he has reached a more suitable age, and of bearing in mind the possible limiting effect of such impairment on the results to be expected from physiotherapy and orthopaedic surgery.

J. B. Stanton

Medical Genetics

240. **A Familial Neuro-ophthalmological Syndrome Apparently Genetically Determined and Possibly Throwing Light on the Problem of Familial Disseminated Sclerosis.** (Syndrome neuro-ophtalmologique familial paraissant génétiquement conditionné et susceptible d'éclairer le problème des scléroses en plaques familiales)
R. COULONJOU, G. RENARD, J. POUDEROUX, and L. NICOLET. *Revue d'oto-neuro-ophtalmologie* [*Rev. Oto-neuro-ophtal.*] **25**, 461–468, Nov.–Dec., 1953. 4 refs.

The authors describe a syndrome which they first encountered in a young woman of 23 who presented with a 3 years' history of intermittent diplopia and weakness in the left lower limb and a 6 months' history of myopia. On examination some cerebellar disturbance, with muscle wasting in the left leg and bilateral adiadochokinesia, was found. Visual acuity was greatly diminished and both optic disks were pale and atrophic, especially in the temporal zone. Peripheral visual fields were normal, but there was an absolute central scotoma of 5 to 10 degrees. Pupillary and corneal reflexes were unimpaired. There was some spontaneous improvement, subjectively and objectively, after 12 months.

Further inquiries into the family history were made, and syndromes similar to the above in their ophthalmological manifestations, differing mainly in the degree of involvement of the central nervous system, were found in a brother and in 3 male first cousins of the patient's mother. The age at the time of onset of symptoms in all these cases was between 19 and 27 years. In addition, a brother of the propositus was feeble-minded and a sister had had recurrent chorea some years previously with no apparent sequelae. One of the cousins was subjected to an exploratory craniotomy, which revealed a hypophyseal band with localized serous meningitis and cerebral softening, and a large arachnoid cyst attached to the chiasma. The acute optic neuritis was thus in this case apparently associated with infection.

The authors discuss the pedigree of this family in the light of recent French literature on the role of heredity in the aetiology of disseminated sclerosis, and refer to the similarities between this syndrome and that of Leber's disease. They tentatively advance a hypothesis of a genetically-determined susceptibility or hypersensitivity of these patients to certain types of infection.

R. H. Cawley

241. **Observations on the Aetiology of Mongolism**
L. S. PENROSE. *Lancet* [*Lancet*] **2**, 505–509, Sept. 11, 1954. 2 figs., 46 refs.

Ever since mongolism was recognized as a specific abnormality in 1866 by Langdon Down it has provided fertile ground for speculation and investigation, but its cause still remains a mystery. It is one of the commonest types of mental deficiency, occurring approximately once in every 600 births in European populations, while it also occurs, though apparently less commonly, in African, Indian, Chinese, and Japanese populations. Whereas it has been repeatedly shown that the incidence of mongolism increases sharply with rising maternal age after the 30th year, no consistent association has been found between mongolism and maternal ill health before and during pregnancy. Paternal age and order of birth appear to be of no significance. Fraternal (dizygotic) twins are only exceptionally both affected, but whereas many cases have been reported in which both of a pair of identical (monozygotic) twins were mongols, there is no proven case of only one of such twins being affected. The incidence of mongolism among the brothers and sisters of mongols is probably slightly, though definitely, higher than among the general population, but there have been many instances reported of families in which 3 sibs have been affected, and at least one case of 4 and one of 5 affected sibs, so that there can be little doubt that " mongolism does show a genuine tendency to familial concentration in spite of the fact that the vast majority of cases give no indication of this trend ".

The mother's age at the birth of the mongol tends to be lower in cases in which she has a relative who is also a mongol. It is probable therefore that some mothers, by virtue of an inherited predisposition, are especially likely to have mongol offspring. Confirmation of this is provided by the finding that the mothers and sibs of mongol children have a slight but definite tendency to possess certain of the signs of mongolism. This has been shown most conclusively by the author in respect of the *t* triradius on the palm of the hand, the position of which in relation to other points on the palm can be accurately measured. This was found to lie in an unusually distal position in 87% of 253 mongols and in only 11% of 2,046 normal individuals, but this characteristic was found in 16% of 427 parents and 23% of 309 sibs in families containing one or two mongols. The tendency was even more marked among the parents and sibs in those families containing two mongol children, the distal *t* triradius being present in 7 out of 19 mothers, 2 out of 14 fathers, 7 out of 17 sisters, and 7 out of 13 brothers, giving a total incidence of 36·5%. On the other hand there is no evidence that parental consanguinity is a causative factor in mongolism.

After a discussion of the genetic background of mongolism and the possible influence of the maternal genotype the author reaches the following conclusions. " In so far as hereditary differences between different children are part causes, they must depend upon common genes, possibly of several alternative kinds. Some of these genes may be the same as those which influence predisposition in the mother. Abnormal cytoplasm is not likely to be the sole cause, nor is fresh mutation considered a probable explanation. The precipitating environmental influences . . . require intensive investigation."

C. O. Carter

Public Health

242. **Effect of Fluoride in Drinking Water on the Osseous Development of the Hand and Wrist in Children**
H. B. McCauley and F. J. McClure. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] **69**, 671–683, July, 1954. 5 figs., 39 refs.

Exposure to fluoride in drinking water was studied for evidence of detrimental effects on skeletal calcification and bone development in children. Three groups of children aged 7 through 14 years, living in Lubbock and Amarillo, Texas, and Cumberland, Maryland, were selected on the basis of continuous exposure to their communal drinking waters, which contained fluoride in the amounts of 3·5 to 4·5 p.p.m. F, 3·3 to 6·2 p.p.m. F, and 0·1 p.p.m. F, respectively. Radiographs were taken of the right hand and wrist of 2,050 children. From these *x* rays, the skeletal age was assessed and a quantitative index of ossification was determined.

No evidence, available by radiographs, was obtained which would indicate that there was any adverse effect on the carpal bones or on their growth and development as a consequence of the continuous use of drinking water containing approximately 3·5 to 6·2 p.p.m. F. These results confirm the safety of maintaining the fluoride level of public water supplies at about 1·00 p.p.m. F, by controlled fluoridation, for the reduction of tooth decay.—[Authors' summary.]

243. **Fluorine in Subterranean Waters of the U.S.S.R. as a Factor in the Incidence of Fluorosis and Caries.** (Фтор в подземных водах РСФСР как фактор заболеваемости населения флюорозом и кариесом)
S. N. Cherkinsky and R. M. Zaslavskaya. *Гигиена и Санитария* [*Gigiena*] No. 5, 22–26, May, 1953. 2 refs.

The authors have analysed the fluorine content of the water supplies of 198 principal localities and 349 workers' settlements, such as collective farms, in various parts of Russia, a total of 1,455 sources being investigated in all. The fluorine content was low in most cases, being below 0·5 parts per million (p.p.m.) in 96·9% of 133 open reservoirs, in 88·5% of 323 wells and springs, and in 67·8% of 999 artesian wells, but it exceeded 1 p.p.m. in 0·9, 3·4, and 21% of these 3 types of source respectively, a high fluorine content being found most frequently in water coming from geological strata of the Middle Carboniferous age.

The incidence of dental defects was then investigated in 12,000 schoolchildren who were permanent residents of 16 inhabited areas known to be endemic foci of fluorosis. Mottling of the enamel of 1st and 2nd grades of severity was found in 1·2% of 1,005 children consuming water with a fluoride content less than 0·2 p.p.m.; at fluoride concentrations of 0·9 to 1·25 p.p.m. the incidence rose to 15·8% of 82 children, and to 84% of 624 children (including cases of mottling of Grades 3 and 4) at concentrations of 3·8 to 4·65 p.p.m. The incidence of caries in the same groups was found to be 41% in 899 children consuming water containing fluoride in a concentration of 0·07 to 0·2 p.p.m.; at higher concentrations ranging from 3·8 to 4·64 p.p.m. the incidence fell to 16·9% of 624 children, but there was not always a clear correlation between incidence and fluoride concentration. From these observations the authors conclude that the optimal concentration of fluoride which would prevent the development of both fluorosis and caries is evidently about 1·4 p.p.m. There was some evidence that a high consumption of fresh vegetables protected against mottling, probably owing to the relatively high concentration of fluoride in these foods. *D. J. Bauer*

244. **The Relationship between Human Smoking Habits and Death Rates. A Follow-up Study of 187,766 Men**
E. C. Hammond and D. Horn. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 1316–1328, Aug. 7, 1954. 9 figs., 11 refs.

On behalf of the American Cancer Society the authors, with the aid of 22,000 volunteer helpers, have undertaken a large-scale prospective inquiry into the relationship between smoking habits and the death rate from various causes. During the early part of 1952 these helpers interviewed a total of 204,747 white men aged between 50 and 69 and filled in questionaries relating to their smoking habits. On November 1 in each subsequent year the assistants reported whether or not the men they interviewed were still alive and the State Health Departments were asked to provide details of the certified causes of death of those who had died.

The preliminary results now reported relate to 4,854 men known to have died out of 187,766 men interviewed between January 1 and May 31, 1952, for whom the questionaries were adequately completed and who were followed until November 1, 1953. They show that the death rate from all causes was 52% higher among men who had given a history of regular cigarette smoking than among non-smokers, whereas among men who had smoked only cigars or pipes the rate was only 6% higher. Except in the age group 65 to 69, the rate also increased progressively with the number of cigarettes smoked per day. Nearly half the excess mortality among cigarette smokers was attributable to coronary disease; among smokers of more than one packet of cigarettes a day the mortality from coronary disease was about double that among non-smokers. Most of the rest of the excess was accounted for by an increased mortality from cancer. The data are insufficient to determine conclusively whether the death rate from any other disease was also related to smoking, but it is estimated that " lung cancer deaths are from 3 to 9 times as common among men with a history of cigarette smoking as among men who have never smoked regularly and . . . are 5 to 16 times as common among men who smoke one pack or more

per day". The number of deaths recorded from cancer of other specific sites was too small for any definite conclusions to be drawn, but in some cases the impression was obtained that the death rate among regular cigarette smokers was again higher than among non-smokers. The inquiry continues. *R. Doll*

EPIDEMIOLOGY AND IMMUNIZATION

245. **The Spread of Poliomyelitis. An Analysis of Contact during Epidemic Periods**
R. S. PAFFENBARGER, V. O. WILSON, D. BODIAN, and J. WATT. *American Journal of Hygiene* [*Amer. J. Hyg.*] 60, 63–82, July, 1954. 3 figs., 22 refs.

On the basis of observations made during epidemics of poliomyelitis in Olmsted County, Minnesota, in 1952, and in Hidalgo County, Texas, in 1948 and 1950, which are described in detail, the authors discuss here certain quantitative aspects of contact in the transmission of the disease. For the purpose of this study "contact" is defined as "personal association between a potential source case and another individual in a home or on home premises at any time during a 7-day period, from 3 days before to 3 days after the date of onset of the case".

In the Olmsted County epidemic 215 cases occurred among 49,000 residents, and 3,752 individuals were reported to have been in contact with poliomyelitis, an average of 17·4 for each case. Among these contacts 50 cases of poliomyelitis developed, an attack rate of 1·3% compared with a computed attack rate among non-contacts of 0·6%. The median incubation period was 10 days with an 80-percentile range of 5 to 33 days. The attack rate among other members of households in which a case had occurred was 2·6% compared with a rate for the county of 0·4%, and it is concluded that the risk of contracting poliomyelitis varies directly with the degree of contact. The attack rates among contacts of paralytic and non-paralytic cases were approximately equal. The results of analysis of data obtained retrospectively from the Hidalgo County epidemics were substantially the same.

During the course of the epidemic in Olmsted County the age distribution of cases changed, the younger age groups predominating at first and the older predominating later, but the data are insufficient for any firm conclusion to be drawn concerning the cause of this phenomenon. *Benjamin Schwartz*

246. **Poliomyelitis Infection in Households. Frequency of Viremia and Specific Antibody Response**
D. BODIAN and R. S. PAFFENBARGER. *American Journal of Hygiene* [*Amer. J. Hyg.*] 60, 83–98, July, 1954. 29 refs.

During epidemics of poliomyelitis in Olmsted County, Minnesota, and in Baltimore City and County, Maryland, in the summer of 1952, samples of serum were obtained from child contacts in households in which a case had been diagnosed as soon as possible after the onset of the index case and again one month later. Attempts were made to isolate virus from all first specimens and all sera were tested for antibodies against the three known types of poliomyelitis virus.

In all, sera from 132 contacts were tested and in 33 of these children, termed "converters", the titre of antibody against Type-1 virus increased at least 10-fold during the observation period. Of the remainder, in 81 the titre exceeded 1 in 100 in both specimens and these contacts were therefore considered immune, while 18 children had no demonstrable antibody in either specimen. It is noted that the first specimen was obtained before the fifth day after the onset of the index case in two-thirds of those cases in which a rise in titre occurred. The first sample from 9 of the converters contained no antibody, and Type-1 (Brunnhilde) poliomyelitis virus was isolated from 5 of these on inoculation into roller-tube tissue cultures. Four of these children developed symptoms of abortive poliomyelitis within a few days, and one remained symptom-free. Serum from 2 children who developed paralytic poliomyelitis one and 3 days respectively after the initial bleeding already contained substantial levels of Type-1 antibody. It is suggested, therefore, that the interval between the initial viraemia and the onset of paralytic poliomyelitis is of the order of 2 to 5 days.

The authors point out that the frequency with which the virus was isolated from the blood of contacts without subsequent development of paralysis strengthens the supposition that poliomyelitis in anthropoid hosts is not strictly a neural disease. They suggest that the initial infection in a family is usually in a child and unrecognized, this child becoming the source of infection for other members of the household. *Benjamin Schwartz*

247. **An Illness Resembling Poliomyelitis Observed in Nurses**
A. D. MACRAE and J. F. GALPINE. *Lancet* [*Lancet*] 2, 350–352, Aug. 21, 1954. 1 fig., 9 refs.

During the poliomyelitis epidemic of 1953, 205 confirmed or suspected cases were admitted to Whitley Hospital, Coventry. Of the 49 members of the medical, nursing, and physiotherapy staffs who were in contact with these patients, 13 fell ill with symptoms resembling those of poliomyelitis—sore throat, headache, backache, pyrexia, and paresis of varying degree—but also including sensory disturbances, tenderness of the muscles, and normal or temporarily diminished tendon reflexes. Examination of the cerebrospinal fluid did not reveal any abnormality, attempts to isolate a virus from the faeces were unsuccessful, and although in most of the sera tested multiple antibodies against the poliomyelitis viruses were present, there was no increase in their titre during the illness. Recovery was complete within 1 or 2 months. The authors conclude that this outbreak, despite its close association with the epidemic of poliomyelitis, was probably not due to the poliomyelitis virus and that its cause remains unknown.

[The clinical picture in these cases is very suggestive of Coxsackie virus infection, but no serological tests for these viruses appear to have been carried out.]
Franz Heimann

248. **Non-paralytic Poliomyelitis**
D. THOMSON. *Monthly Bulletin of the Ministry of Health* [*Monthly Bull. Minist. Hlth* (*Lond.*)] **13**, 76–89, May, 1954. 1 fig., 38 refs.

Non-paralytic poliomyelitis was first recognized as a clinical entity at the end of last century, and, since then, the part which it plays in the epidemiological pattern of the infection has come to be increasingly appreciated. This form of the disease has had to be notified separately, in England and Wales, during the past 4 years, and analysis of such notifications suggests that, on occasion, they may have included cases of other acute benign neurotropic infections. The proportion of paralytic to non-paralytic cases notified reveals certain anomalies in relation to geographical, age, and sex-distribution. Until a simple diagnostic test for non-paralytic poliomyelitis is devised, it may be advisable to use only notifications of paralytic cases in studies of the comparative incidence of the infection. Nevertheless, the epidemiological value of the detection of non-paralytic cases is considerable.—[Author's summary.]

249. **Further Investigation into the Association between Immunizing Injections and Paralytic Poliomyelitis**
A. M. PEACH and A. J. RHODES. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **44**, 1185–1188, Sept., 1954. 10 refs.

250. **The Effect of Gamma Globulin on Subclinical Infection in Familial Associates of Poliomyelitis Cases. I. Quantitative Estimation of Fecal Virus**
G. C. BROWN, A. S. RABSON, and J. H. SCHIEBLE. *Journal of Immunology* [*J. Immunol.*] **73**, 54–61, July, 1954. 31 refs.

In the summer and fall of 1953, family associates of reported cases of poliomyelitis were inoculated with gamma globulin as a possible prophylactic measure. Fecal specimens were collected at 3-weekly intervals from 135 individuals in 29 families, most of whom had received twice the amount (0·28 ml./lb. [0·6 ml. per kg.]) of gamma globulin. Four of 64 individuals (6%) in families of questionable cases from whom no virus could be isolated were found to be positive for virus. In contrast, 29 of 70 persons (41%) in families of confirmed poliomyelitic cases were undergoing subclinical infection. The quantity of fecal virus was determined by direct titration in Hela cell type tissue cultures. The specimens of some individuals were infective in dilutions as high as 10^{-6}.

Virus was found to persist during the period of study in essentially the same titer in most individuals. Nine persons with low titered virus became negative, but 5 who were originally negative for virus developed subclinical infection with high titered virus although the gamma globulin had been administered over a week before.

From these data it would appear that subclinical infections, when present at the time of inoculation, were usually not affected by gamma globulin nor were they necessarily prevented from developing during the week after its administration. The significance of these data and their possible applications to the phenomenon of passive-active immunization against poliomyelitis are discussed.—[Authors' summary.]

251. **An Outbreak of Infectious Hepatitis Apparently Transmitted through Water**
C. B. TUCKER, W. H. OWEN, and R. P. FARRELL. *Southern Medical Journal* [*Sth. med. J.* (*Bgham, Ala.*)] **47**, 732–740, Aug., 1954. 2 figs., 10 refs.

The authors describe investigations into an explosive outbreak of gastroenteritis followed by infective hepatitis which occurred in a holiday camp in Tennessee and was apparently water-borne. The gastroenteritis affected simultaneously 122 persons among a camp population of 291, an attack rate of 41·9%. The campers were sent home 4 days after the outbreak started, and 102 of them developed infective hepatitis later, the incidence of hepatitis thus being 35·1%. The families of all campers and staff members who had been at the camp during the relevant period were followed up for a period of 3 months after the onset of the primary cases. Some of the members of these families had been given serum globulin, and no secondary cases occurred among these, whereas 13 secondary cases occurred among the 247 contacts who had not been immunized, giving a secondary attack rate of 5·3%; this comparatively low rate is attributed to the comparatively high economic status of the families and the high standard of personal hygiene in their homes. The incubation period of infective hepatitis varied between 22 and 46 days in primary and between 15 and 38 days in secondary cases. The attack rate in the age group 10 to 19 years, which included the majority of the campers, was higher than among the older persons in the camp, who were mostly members of the camp staff.

Various channels of infection were investigated, and the water supply of the camp, derived from a spring, was found to be liable to contamination through a fault in the sewage system. Samples of unchlorinated water taken on several occasions had high bacterial counts and coliform organisms were present. When the main sewer was plugged near its outlet into a septic tank and fluorescein flushed through the soil pipes of 3 of the camp buildings which were above and close to the spring, the dye reached the spring water within 70 minutes. Further tests traced the leakage to the earthenware pipe connecting the building nearest the spring to the main camp sewer, which was of metal. The spring was adequately protected from surface contamination and the supply was chlorinated, but Neefe *et al.* (*J. Amer. med. Ass.*, 1945, **128**, 1076) are quoted as having shown that the usual amount of chlorine used in treating water supplies does not inactivate or attenuate the virus of infective hepatitis. Among the 26 persons who occupied the building with the faulty sewer connexion during the relevant period were 2 boys who had been exposed to infective hepatitis 2 to 3 months previously. It is postulated that one of these might have had a mild or subclinical attack and been excreting the virus during the time he was at the camp. *J. Cauchi*

Industrial Medicine

252. **Raynaud's Phenomenon in Workers with Vibratory Tools**
R. P. JEPSON. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **11**, 180–185, July, 1954. 18 refs.

An investigation was carried out at the Royal Infirmary, Manchester, to determine whether patients suffering from Raynaud's phenomenon as the result of using vibratory tools can be distinguished from normal subjects and from those in whom the condition is due to some other cause. The 34 patients examined were employed in a wide variety of occupations involving vibration. The onset of the condition followed a symptomless period of work with a pneumatic tool which ranged from one month to 20 years. Not all exposed workers developed Raynaud's phenomenon, but some, such as flangers and clinchers in the motor industry and shoe pounders, were particularly liable, symptoms often being noted within the first year. The fingers first affected were those most exposed to vibration. The symptoms appeared to reach a peak in their severity; thereafter they did not progress but persisted unchanged, even if the patient left the industry concerned. *X*-ray examination revealed carpal or metacarpal cysts in only 4 of the 34 patients. In all the patients there was a normal reaction to the hyperaemia test; 14 developed white " dead " fingers when the hands were immersed in a water bath at 15° C. for 15 minutes. The response to the heat-flow test, carried out with a copper–tellurium heat-flow disk, was normal in 13 out of 24 of the patients compared with 8 out of 29 healthy controls.

The author concludes that the diagnosis of Raynaud's phenomenon caused by vibratory tools must at present be made on clinical grounds. *John Pemberton*

253. **Tumour of the Urinary Bladder as an Occupational Disease in the Rubber Industry in England and Wales**
R. A. M. CASE and M. E. HOSKER. *British Journal of Preventive and Social Medicine* [*Brit. J. prev. soc. Med.*] **8**, 39–50, April, 1954. 27 refs.

It has already been shown that tumours of the urinary bladder are an occupational hazard among workers in certain sections of the chemical industry, notably among those engaged in the manufacture of a rubber antioxidant containing about 2·5% of free naphthylamine, including a proportion of both the alpha and beta isomers (*Brit. J. industr. Med.*, 1954, **11**, 75; *Abstracts of World Medicine*, 1954, **16**, 256). An investigation was therefore undertaken at the Chester Beatty Research Institute, London, to determine whether the risk extends into the " rubber occupations " as defined in the occupational tables of the Registrar-General's Census Reports for 1924 and 1934. From the previous investigation tumours due to this cause would be expected to develop only after an induction period of 18 ± 7 years. As the antioxidant was first introduced about 1927–8, no increase in deaths from tumours of the bladder would be therefore expected before 1935. From estimates of the population at risk during the period 1921–35 the expected number of deaths from this cause was 8·5, whereas in fact there were 9. On the other hand, in the period 1936 to 1951 the expected number was 15·9 and the actual was 26. Thus the standardized mortality ratio was 106 for the period 1921–35 and 164 for the period 1936–51, the excess being statistically significant.

In one county borough, an important centre of the rubber industry, the expected number of deaths from cancer of the bladder in the period 1936–50 was 2·6, whereas there were actually 5—a standardized mortality ratio of 192. The records of all hospitals in this county borough were also studied, and it was found that whereas the expected number of reported cases of bladder tumour among males engaged in rubber occupations was 4·0, the number found was 22, giving a standardized " report " ratio of 550. It would thus seem that the statement that there is a definite excess of cases of bladder tumour in workers in rubber occupations in this county borough can be made with considerable confidence.

These findings are consistent with, but do not prove, the hypothesis that the risk of occupational tumour of the bladder was introduced into the industry with the antioxidant containing naphthylamine. However, it is reported that " when the trend of these studies became known, the manufacturers of the antioxidant voluntarily ceased its manufacture and withdrew it from their range of products, and the rubber industry immediately discontinued the use of the antioxidant and destroyed old stocks ". *K. M. A. Perry*

254. **Tumours of the Urinary Bladder in Workmen Engaged in the Manufacture and Use of Certain Dyestuff Intermediates in the British Chemical Industry. Part II. Further Consideration of the Role of Aniline and of the Manufacture of Auramine and Magenta (Fuchsine) as Possible Causative Agents**
R. A. M. CASE and J. T. PEARSON. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **11**, 213–216, July, 1954. 10 refs.

In the first part of this paper from the Chester Beatty Research Institute, London (*Brit. J. industr. Med.*, 1954, **11**, 75; *Abstracts of World Medicine*, 1954, **16**, 256) the authors presented and discussed the statistical evidence which had been collected about the relation of the dyestuff intermediates aniline, benzidine, α-naphthylamine, and β-naphthylamine to occupational tumours of the urinary bladder. The conclusion was reached that the manufacture and use of aniline were probably not a cause of the disease, but that certain workers who were employed in the manufacture of magenta (fuchsine), in which process aniline is necessarily used, might be in some danger of developing occupational bladder tumours.

It was suggested that the manufacture of auramine, for which purpose aniline is not used, might also be a source of the same danger, and a more detailed investigation of the occurrence of bladder tumours among workmen exposed to these substances, which are not intermediates but finished dyes, was therefore undertaken, the results of which are reported here.

Nominal rolls of workmen engaged in the manufacture of auramine and magenta were compiled and classified as follows: (*a*) those who had had contact, in manufacture or use, with aniline but not with magenta, auramine, benzidine, or α- or β-naphthylamine; (*b*) those who had manufactured magenta, but who had not come into contact with auramine, benzidine, or α- or β-naphthylamine; (*c*) those who had manufactured auramine, but who had not manufactured magenta or come into contact with benzidine or α- or β-naphthylamine; (*d*) a small group of men who had manufactured both auramine and magenta, but who had not come into contact with benzidine or α- or β-naphthylamine. The data for each of these classes were then analysed by the special statistical methods recorded in Part I.

The authors conclude that no statistical evidence has been found to suggest that the manufacture or use of aniline in the British chemical industry between 1910 and 1952 has caused occupational tumours of the bladder. (It is emphasized, however, that this conclusion does not necessarily conflict with the observations of other authors in other countries or in earlier times.) On the other hand the manufacture of auramine and magenta in the British chemical industry during the same period appears to have involved a definite occupational hazard in respect of tumour of the urinary bladder, a statistically significant excess of deaths certified as being due to bladder tumour being found, and the age of onset of, and death from, the disease in workers engaged in these manufacturing processes being earlier than in the general population.

It is pointed out, however, that the statistical analysis was not capable of determining the causal factor, and that it should not be assumed that the finished products are necessarily dangerous. *A. Meiklejohn*

Correction.—In the abstract of the first part of this paper (see reference above) the last sentence at the foot of column one should read as follows: "The induction time appears to be a characteristic of the causal agent, as it is uninfluenced by the severity and duration of exposure. It was also found that short exposures of less than a year carry a definite risk". —EDITOR.

255. **Aplastic Anaemia due to Trinitrotoluene Intoxication**

M. A. DOBBIN CRAWFORD. *British Medical Journal* [*Brit. med. J.*] **2**, 430–437, Aug. 21, 1954. 2 figs., 11 refs.

A total of 27 cases of toxic anaemia and toxic purpura attributable to poisoning with trinitrotoluene (TNT), which occurred in the United Kingdom between 1940 and 1946 are reported in this paper from the Department of the Chief Medical Officer, Ministry of Supply, London. In 24 of the cases, 15 of which were fatal, the diagnosis was aplastic anaemia due to TNT; in the remaining 3 symptoms and signs were atypical and mild. The occupational and metabolic aspects of the intoxication are briefly discussed, and the clinical manifestations are described as cyanosis, dermatitis, anilism, toxic jaundice, toxic anaemia, and toxic purpura, roughly in that order of frequency.

The blood picture, which was frequently complicated by haemorrhage from various sites, showed normocytic or macrocytic anaemia, with, in some cases, anisocytosis. The erythrocyte count varied from 630,000 to 3,504,000 per c. mm.; occasional erythroblasts were seen in 2 cases, and in the few cases in which films were stained for reticulocytes the number varied from 0 to 4% of the erythrocytes. Stippled cells were found in one fatal case and in one non-fatal case; target cells were seen in 4 cases. Haemoglobin varied between 12 and 70% and the colour index was raised at some time in the majority of the cases. The leucocyte count varied from 300 to 6,200 per c. mm. The differential leucocyte count was determined in only 12 of the fatal cases; in 4 of these neutrophils formed 0 to 4% of the leucocytes (agranulocytosis); in the remainder there was a varying degree of granulocytopenia, which was also observed in some of the patients who recovered. Of 3 cases in which sternal puncture was performed the bone marrow was aplastic in 2, the findings being inconclusive in one. The necropsy findings in 11 out of 12 cases for which these were available showed that the marrow on macroscopical examination was aplastic. Of 7 of the patients who recovered, the marrow on sternal puncture was aplastic or hypocellular in 4; in the remaining 3 it showed a hyperplastic reaction. Evidence of liver damage was found in 10 of the 15 fatal cases.

The clinical aspects of the intoxication are discussed, with particular reference to the insidious onset of the anaemia. Several cases are described in detail. The author states that early and complete removal of the patient from exposure to TNT is the first essential in treatment. Blood transfusion was frequently necessary, a satisfactory regimen being an initial transfusion of 2 or 3 pints (1·1 or 1·7 litres) followed by transfusion of 3 or even 4 pints (1·7 or 2·3 litres) during convalescence; the patient was then sent home for a month or longer, returning for examination and for further treatment if the blood level was not maintained. Restoration of haematopoiesis was encouraged by the administration of liver, iron, and "vitamins B, C, and K". *P. N. Magee*

256. **Acute Poisoning from the Ingestion of Trichlorethylene.** (Intoxication aiguë par ingestion de trichloréthylène)

A. RAVINA, M. PESTEL, Y. TROCMÉ, and P. TCHERDAKOFF. *Presse médicale* [*Presse méd.*] **62**, 1405–1406, Oct. 16, 1954.

257. **Anginal Attacks in Workers Employed in the Production of Dynamite and Nitroglycerine.** (Attacchi stenocardici nei lavoratori addetti alla produzione delle dinamiti con nitroglicole)

M. BARSOTTI. *Medicina del lavoro* [*Med. d. Lavoro*] **45**, 544–548, Oct., 1954. 3 refs.

Forensic Medicine and Toxicology

258. **A Method for Determining the Age of Blood and Seminal-fluid Stains.** (Eine Methode zur Altersbestimmung von Blut- und Spermaflecken)
E. WEINIG. *Deutsche Zeitschrift für die gesamte gerichtliche Medizin* [*Dtsch. Z. ges. gerichtl. Med.*] **43**, 1–10, 1954. 2 figs., 15 refs.

Working at the University Institute of Forensic Medicine and Criminology, Erlangen, the author has used the migration of chlorine ions from blood stains into the surrounding material as a means of studying the age of blood stains, the method being adapted from that used to determine the age of ink-marks on paper. Its application to the determination of the age of blood stains is facilitated by the relative constancy of the blood chloride concentration. The " chloride picture " is discussed in relation to the quality and properties of the paper or other material on which it is studied and to the environmental conditions, especially humidity, since increase of temperature and of humidity both favour migration of the chloride ions. The method has further been adapted to the study of blood stains on cotton, wool, and artificial silk; the method is reliable except in conditions of extreme atmospheric humidity.

A similar method was applied to the study of the stains caused by seminal fluid on the various textiles used in the manufacture of underclothing and of handkerchiefs, special consideration being given to the influence of body temperature and body humidity. The degree of chloride migration was here subdivided into eight stages, the first three depending on the accentuation of chloride ion concentration at the margin of the stain, and the others being related to the distance to which the chloride ions have migrated. Whereas extreme humidity invalidates the chloride method for blood stains, this condition can be utilized in the investigation of seminal-fluid stains by studying the " sulphate picture ", since sulphate ions do not ordinarily migrate from seminal stains (nor from ink stains) except under conditions of extreme humidity. A method for the determination of the sulphate content and distribution is described. Finally, it is pointed out that by these methods the age of stains due to vaginal secretions or any fluid containing chloride and sulphate ions may also be determined. *Ferdinand Hillman*

259. **Abuse of Alcohol and Alcoholic Positional Nystagmus.** (Alkoholmissbrauch und Alkohollagenystagmus)
H. W. WALTER. *Deutsche Zeitschrift für die gesamte gerichtliche Medizin* [*Dtsch. Z. ges. gerichtl. Med.*] **43**, 232–241, 1954. 1 fig., 17 refs.

In an attempt to put the clinical examination of persons suspected of drunkenness on an objective basis, the author describes the phenomenon of " alcoholic positional nystagmus " and reports the results of experimental investigations carried out at the University of Cologne. Alcoholic positional nystagmus occurs constantly after the consumption of a critical amount of alcohol which, although varying with individual tolerance, has a maximum value equivalent to 60 ml. of absolute alcohol. The phenomenon cannot be suppressed by voluntary effort, especially if the subject is provided with +12D lenses to prevent fixation, and its presence always indicates that the individual's alcohol tolerance has been exceeded.

It occurs in three stages. (1) This is seen with the subject lying on one side, when a lateral nystagmus occurs, the quick component of which is directed towards the side on which the patient is lying. The direction is of course reversed when the subject turns over. This stage is first seen 79 ± 43 minutes after beginning to drink and lasts for some 216 ± 50 minutes after drinking ceases. (2) The neutral period, during which no nystagmus is observed, follows next and lasts 55 ± 19 minutes. (3) This consists in positional nystagmus in the reverse direction, that is, with the quick component directed away from the side on which the subject is lying. This appears some 4 to 5 hours after drinking has ceased and gradually subsides over a period of 10 to 16 hours. These three stages are not correlated exactly with points on the blood alcohol curve, but Stage 1 usually begins when the concentration of alcohol in the blood has reached 0·06% (60 mg. per 100 ml.). The mechanism, differential diagnosis from positional nystagmus due to other causes, and forensic importance of alcoholic positional nystagmus are discussed and the author concludes that blood alcohol determination and testing for the presence of positional nystagmus together give a very reliable objective means of estimating the degree of intoxication and incapacity. *J. B. Stanton*

260. **Blood Grouping Tests in Disputed Paternity Proceedings. Studies with A-B-O, M-N, and Rh-Hr Factors**
L. N. SUSSMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **155**, 1143–1145, July 24, 1954. 13 refs.

The value of blood grouping in the solution of medico-legal problems has been firmly established, and the laws governing the inheritance of the characters that determine the blood type have been proved by thousands of family studies. In the U.S.A. the exclusion of parentage on the basis of a blood test is legally decisive in the States of New York, Maine, and New Hampshire, while in other cities and States the results are admissible in evidence and the performance of such tests may be ordered by the Court. The present author states that in medico-legal practice blood grouping is limited at present to 3 systems of blood factors, namely, the ABO, MN, and Rh-Hr systems, and although by the use of all available tests about 50,000 individual varieties of blood can be distinguished, using the systems enumerated above 216 varieties of blood are demonstrable, and the chance

of exclusion of paternity in a case of false accusation is 50%. The author postulates certain desiderata bearing on blood grouping in disputed paternity, namely, certain identification, use of potent sera, expert training and experience on the part of the operator, positive and negative controls, and the duplication of tests where possible. The author next gives details of 100 consecutive cases dealt with and tabulates the findings in the 21 cases where exclusion was achieved. He makes a plea for the extended use by legal authorities of blood grouping in affiliation cases. *Gilbert Forbes*

261. **Toxicity of Chlorsulphonic Acid–Sulphur Trioxide Mixture Smoke Clouds**

G. R. CAMERON. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 197–204, 1954. 3 refs.

The harmful effects of the fog which London experienced from Dec. 5 to Dec. 8, 1952, have been attributed to abnormal contamination of the atmosphere with oxides of sulphur, especially sulphur trioxide (SO_3). The present author reports animal experiments carried out at the Chemical Defence Experimental Establishment, Porton, in 1943, and discusses the results with reference to the possible effects of chlorsulphonic acid fumes on human beings.

Monkeys, goats, rabbits, rats, mice, and guinea-pigs were exposed to smoke clouds consisting of particulate sulphuric acid with varying amounts of HCl in the gaseous state. Concentrations of 30 or 60 mg. of SO_3 per c. metre were used, periods of exposure varying. The only animals with symptoms during exposure were guinea-pigs; some died and others showed signs of bronchial spasm, even after short periods in the chamber. When these animals were exposed for longer periods the mortality was high, especially when the higher concentration of vapour was used. No deaths occurred among monkeys, goats, or rabbits, and among the few rats and mice which died there was a high incidence of natural lung disease. It is concluded that these species are relatively insusceptible to the concentrations of SO_3 employed, while the guinea-pig is markedly susceptible.

The main pathological changes were found in the lungs, liver, kidneys, and adrenal glands. The lungs showed bronchial spasm with associated collapse and overdistension, oedema, and acute bronchitis. In the liver there was marked congestion with mild injury of liver cells, and in the kidneys congestion with mild injury of renal tubule cells was observed. The adrenal glands showed congestion with, occasionally, haemorrhage and fatty changes in the cortex. In survivors among animals repeatedly exposed there was evidence of injury to the lungs, but other organs were normal. It is suggested that in most animal species some predisposing factor is necessary before injury can be induced by chlorsulphonic acid fumes. In the susceptible guinea-pig, however, there is a regular sequence of pathological changes—irritation of bronchial and bronchiolar muscle leading to contraction and spasm, followed by pulmonary collapse and oedema, and then by compensatory emphysema. Attention is drawn to the peculiar susceptibility of the guinea-pig to conditions inducing bronchial spasm, which is sometimes very similar to asthma in human beings, and the author tentatively suggests that when human beings are exposed to chlorsulphonic acid fumes the subjects at risk will be those who are susceptible to bronchial spasm. *P. N. Magee*

262. **Death due to Accidental Poisoning in Young Children**

K. BAIN. *Journal of Pediatrics* [*J. Pediat.*] **44**, 616–623, June, 1954. 2 figs., 5 refs.

The publication of a study of the number of deaths from accidental poisoning in young children in England and Wales during the decade 1940–50 by Swinscow (*Arch. Dis. Childh.*, 1953, **28**, 26) prompted the author, working at the Department of Health, Education and Welfare, Washington, D.C., to institute a similar inquiry in the United States for the same period. It was found that whereas the rate in England and Wales for ages 1 to 5 was 0·87 deaths per 100,000 population the comparable figure in the U.S.A. was 3·6 per 100,000. This discrepancy was even larger for children under 1 year of age, for whom the death rates were respectively 0·29 and 1·8 per 100,000 population. Although the incidence in the U.S.A. among the non-white population was three times that in the white population, this factor alone did not account for the observed difference between English and American death rates.

A detailed analysis of causes of death from poison in the 2 years 1949 and 1950 in children under 5 years was therefore undertaken. It was found that there were 834 such deaths, and three groups of poisons were together responsible for most of them—namely, drugs, petroleum products, and external applications. Whereas in England and Wales drugs accounted for about two-thirds of the cases, in the United States only one-third was so caused, aspirin and the barbiturates being the most frequently incriminated; poisoning from preparations of iron, common in Great Britain, is rare in the U.S.A., only 2 cases being reported in the 2 years. The petroleum product kerosene (paraffin) was the most important single poison in the United States, having been responsible for one-quarter of the deaths, in sharp contrast to British findings. The rate among negro children was about six times that in white children for this agent, a fact which is attributed to the widespread use of paraffin as a fuel in the poorer homes. External applications accounted for rather more than another third of the deaths, lead ranking highest, then arsenic, then caustic substances. The death rates from poisoning in certain Southern States of the U.S.A. were twice as high as in the rest of the country, very largely because of an increase in the number of cases of kerosene, arsenic, or corrosive poisoning in those States. The author concludes: " Roughly two-thirds of the deaths from accidental poisoning would be wiped out if aspirin, the barbiturates, kerosene, lye, lead and arsenic were unavailable to small children ". She also comments unfavourably on the inadequacy of the information on the death certificate in about one-seventh (40) of the 276 cases of poisoning due to drugs. *M. MacGregor*

Anaesthetics

263. **Three Phenothiazine Derivatives in Anaesthesia**
R. W. BAXTER, J. A. BOLSTER, and S. MCKECHNIE. *Anaesthesia* [*Anaesthesia*] **9**, 79–87, April, 1954. 1 fig. 13 refs.

The action of three derivatives of phenothiazine—" phenergan " (promethazine), " diparcol " (diethazine), and " largactil " (chlorpromazine)—in potentiating the action of general anaesthetics, inhibiting the autonomic nervous system and thus reducing shock, and preventing vomiting of central origin was investigated at the Royal Northern Infirmary and Raigmore Hospital, Inverness. After some preliminary trials the following technique was adopted. The evening before operation 50 mg. of promethazine and 5 g. of barbitone sodium (" medinal ") were given by mouth; an hour before operation 50 mg. of promethazine, 100 mg. of pethidine, and 1/100 gr. (0·65 mg.) of atropine were given by intramuscular injection; 15 minutes before operation a mixture of 250 mg. of diethazine, 50 mg. of chlorpromazine, and 100 mg. of pethidine in 20 ml. of distilled water was injected slowly until the patient fell asleep. After about 15 minutes anaesthesia was induced if this was considered necessary. There was a significant reduction in quantity of the anaesthetics used at operation and in the amount of postoperative sedation required. Injection of the mixed solution invariably produced a rise in the pulse rate, and the blood pressure was labile and unpredictable, but there was a complete absence of shock during and after operation, and the patient's postoperative condition was good.

A. M. Hutton

264. **Succinyldicholine and Lignocaine by Continuous Intravenous Drip. Report of 1,000 Administrations**
S. G. DE CLIVE-LOWE, P. W. S. GRAY, and J. NORTH. *Anaesthesia* [*Anaesthesia*] **9**, 96–104, April, 1954 3 figs., 15 refs.

The administration of " scoline " (suxamethonium chloride) and " xylocaine " (lignocaine hydrochloride) by intravenous drip to 900 patients undergoing a wide variety of operations is described. Anaesthesia was induced with 0·5 g. of thiopentone and 50 mg. of suxamethonium administered intravenously; this was followed by intubation with a cuffed tube lubricated with 5% lignocaine ointment. Anaesthesia was maintained with nitrous oxide and oxygen and suxamethonium and lignocaine by intravenous drip. The authors state that a dosage of 0·75 g. of lignocaine can be given during the first hour of the operation but that the dosage must be reduced for longer procedures, otherwise toxic symptoms will develop. Convulsions occurred in 3 cases in the series. In 77% of the cases there was some postoperative analgesia, as the lignocaine drip was continued until all dressings had been completed after operation. The suxamethonium drip was discontinued when no further relaxation was required. Initially, complete apnoea developed in patients undergoing abdominal operations, but later the suxamethonium drip was adjusted to maintain relaxation and yet allow adequate respiratory exchange.

There were no deaths attributable to this method of anaesthesia.

A. M. Hutton

265. **Membranous Laryngo-tracheitis following Endotracheal Intubation**
A. P. MUIR and J. STRATON. *Anaesthesia* [*Anaesthesia*] **9**, 105–113, April, 1954. 19 refs.

Of 1,500 patients at the Eastern General Hospital, Edinburgh, who were subjected to thoracic operations involving endotracheal intubation for 1 to 4 hours, 4 developed a laryngeal membrane giving rise to some degree of obstruction in the immediate postoperative period. Discussing the aetiology of the laryngotracheitis in these 4 cases and in 23 reported in the literature, the authors state that trauma in the presence of infection appears to be the primary factor. They do not consider that ischaemic necrosis of the tracheal wall from pressure of the inflated cuff is a likely explanation. They state [rightly] that the pressure required to inflate a cuff is not indicative of the pressure applied to the tracheal mucosa, and they describe experiments proving this. For the treatment of the condition bronchoscopy should be carried out promptly, and because infection is an important factor antibiotics should be given at once.

A. M. Hutton

266. **The Effect of Long-acting Infiltration Anesthesia with Efocaine on the Respiratory Movements at Rest Postoperatively. A Photogrammetric Study**
S. HAGBERG, P. HJELSTRÖM, and J. ADAMSRAY. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **6**, 102–106, 1954. 2 figs., 17 refs.

Impaired respiration, attributed largely to pain from the wound following upper abdominal surgery, is considered to be an important causative factor in postoperative atelectasis. The present investigation, carried out at the Serafimer Hospital, Stockholm, was undertaken to determine whether or not relief of pain reduced this respiratory impairment. Of a group of 20 patients undergoing cholecystectomy via a right oblique incision, 12 were given an infiltration [the site is not stated] of " efocaine ", the other 8 not so treated acting as a control group. The effectiveness of the analgesia was tested by observing the postoperative " pallor reflex " as described by Hagberg (*Acta chir. Scand.*, 1952, **104**, 329) and found to be adequate.

Preoperatively, and for 3 days postoperatively, an estimate was made of the resting respiratory movement of the thorax and abdomen by photographing the vertical movements of glossy pellets gummed to black sheets

fixed on the thorax and abdomen respectively. In all cases, whether efocaine had been given or not, the thoracic movements showed the same reduction, namely, 35%. On the other hand, the abdominal movements in patients receiving analgesia showed a reduction of 47% and in those without analgesia 27%. It is claimed that the application of Student's test shows that the difference between these results for the two groups is not statistically significant.

It is concluded, therefore, that postoperative pain after upper abdominal section produces no significant impairment of resting respiration, though it may impair excessive respiratory movements.

[Many would disagree with the validity of the method used in determining resting respiration. Also, the degree of significance to be attached to the results of Student's test is not stated.] *B. L. Finer*

267. **Prolonged Apnoea after Suxamethonium. A Case Study of Pseudocholinesterase**
J. CALVERT, H. LEHMANN, E. SILK, and W. K. SLACK. *Lancet* [*Lancet*] **2**, 354–356, Aug. 21, 1954. 13 refs.

A chance observation that a patient admitted to the psychiatric unit of Whipps Cross Hospital, London, was hypersensitive to suxamethonium provided an opportunity to study the relationship between dosage of this drug and duration of apnoea and also the blood pseudocholinesterase level before and after administration of this enzyme. It was found that 50 to 75 mg. of suxamethonium caused apnoea for 7 to 11 minutes, compared with the normal duration of 2 to 4 minutes with this dosage. The blood pseudocholinesterase level was 45 units, whereas the normal level is 55 to 120 units. Injection of 117,000 units of the enzyme raised the blood level to 91 units and reduced the duration of apnoea after administration of a further 75 mg. of suxamethonium to 4½ minutes. A preliminary injection of 10 mg. of suxamethonium, the usual test dose, caused no significant increase in the duration of apnoea.
V. J. Woolley

268. **A Pneumoflator Attachment to Boyle's Machine**
T. M. WILLIAMS. *British Medical Journal* [*Brit. med. J.*] **2**, 674–676, Sept. 18, 1954. 2 figs., 6 refs.

Controlled respiration during anaesthesia is often required in abdominal and other operations, and when using a semi-open technique. In this paper the author describes an apparatus which can be attached to the outlet of any standard Boyle's machine and, given a gas flow of 15 litres per minute (for example, 10 litres of nitrous oxide and 5 litres of oxygen), will produce efficient intermittent positive-pressure respiration. During expiration the flow of gases is cut off, so that the actual consumption is from 8 to 9 litres per minute. The salient advantages of the device are: (1) it is immediately available for use; (2) no soda-lime is required, and trichlorethylene can be used; (3) no electrical apparatus is necessary, the gases supplying the motive power; (4) a safety valve blows off at a pressure of 30 cm. of water; (5) air is admitted automatically if spontaneous respirations return and the inspiratory demand exceeds gas flow; (6) the rhythmical movement of a small lever projecting from the apparatus provides visual evidence that the machine is functioning; and (7) the depth and rate of respiration can be varied by two simple controls.

[Those interested are referred to the original paper, and to the author's earlier paper (*Brit. J. Anaesth.*, 1952, **24**, 222), for a more detailed description.]
D. D. C. Howat

269. **Prolonged Local Analgesia with Benzocaine-Urethane Solution**
J. KOHN, A. G. RUTTER, and M. VITALI. *British Medical Journal* [*Brit. med. J.*] **2**, 682–684, Sept. 18, 1954. 15 refs.

The authors, at Queen Mary's Hospital, Roehampton, have used a benzocaine–urethane solution to produce analgesia after gastrectomy (60 cases) and to relieve the pain from amputation neuromata (60 cases), with satisfactory results. The preparation and sterilization of the solution, which is a simple one, are described. The *p*H is close to that of tissue fluids, and the solution is therefore less irritant than other long-acting analgesic solutions. Viscosity is low, which makes the solution easy to handle with a normal dry syringe and needle. Nevertheless, a warning is given against shallow injection —that is, into the dermis—and against injecting more than 1 ml. into any one site for depot purposes.

In the patients who had undergone gastrectomy a bilateral midaxillary intercostal nerve block was performed. These patients needed considerably fewer injections of a sedative in the first 3 postoperative days than did a control series. The results in the patients with amputation neuromata were reasonably satisfactory, though the authors admit that these cases do not provide very satisfactory test material.

It is claimed that for the production of relatively long analgesia benzocaine–urethane solution has many advantages over other preparations at present available.
Ronald Woolmer

270. **The Effect of Barbiturates in Patients with Liver Disease**
J. T. SESSIONS, H. P. MINKEL, J. C. BULLARD, and F. J. INGELFINGER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 1116–1127, Aug., 1954. 1 fig., 14 refs.

Pentobarbital in hypnotic doses was given to patients with severe liver disease and to control subjects. The effects of the drug were studied by clinical observations, liver function tests, and measurement of barbiturate blood levels.

No evidence was obtained that patients with liver disease were more sensitive to single injections of pentobarbital, or that the early removal of the drug from the blood of these patients was delayed. Prolonged administration of pentobarbital to patients with decompensated liver disease did not appear to retard recovery in 12 of 13 trials.

The use of sedatives in patients verging on hepatic coma is not recommended, but the specific dangers ascribed to barbiturates in patients with liver disease appear to have been overemphasized.—[Authors' summary.]

Radiology

271. **Effects of *X*-irradiation on the Hypothalamus: A Possible Explanation for the Therapeutic Benefits following *X*-irradiation of the Hypophysial Region for Pituitary Dysfunction**

A. ARNOLD. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **14**, 859–868, Aug., 1954. 5 figs., 20 refs.

Irradiation of the pituitary gland has given useful results in, for example, cases of malignant exophthalmos and in gynaecological conditions, but the gland itself is regarded as relatively radio-resistant, no definite histological changes having been found even after high dosage. In view of the known important role of the hypothalamus in pituitary control, however, the authors, working at the University of Illinois College of Medicine, have irradiated this region in a series of monkeys, 23 megavolt *x* rays from a betatron being used, with a single field (temporal or frontal) 1·0 or 2·5 cm. in diameter; the dosage throughout the hypothalamic area was approximately uniform.

The detailed study of 6 brains 6 months after one single such irradiation showed definite changes almost selectively affecting the paraventricular and supraoptic nuclei of the hypothalamus. A tissue dose of 1,500 r produced moderate changes, but one of 3,000 r produced gross degeneration, deficiency of cells, and defective glial reactivity. Higher doses (5,000 to 7,000 r) caused serious damage to the entire hypothalamus and the cortex.

It seems a reasonable conclusion that some at least of the reported beneficial effects of pituitary irradiation may have been due to effects of such irradiation on the hypothalamus. (Further studies are in progress to determine whether late histological changes occur in the pituitary gland itself.) *J. Walter*

RADIOTHERAPY

272. **Carcinoma of the Paranasal Sinuses and the Nasal Cavities. A Clinical Study of 379 Cases Treated at Radiumhemmet and the Otolaryngologic Department of Karolinska Sjukhuset, 1940–1950.** [In English]

L. G. LARSSON and G. MARTENSSON. *Acta radiologica* [*Acta radiol.* (*Stockh.*)] **42**, 149–172, Aug., 1954. 9 figs., 22 refs.

A report is presented from Radiumhemmet and Karolinska Sjukhuset, Stockholm, on the treatment of carcinoma of the paranasal sinuses and nasal cavities during the period 1940–50. Of 379 such cases seen, 45 were not treated; the sex incidence was equal and the patients' ages ranged from 19 to 80. In view of a history of previous chronic infection in 14·5% of cases the prolonged conservative treatment of chronic sinusitis is deprecated. In 33 cases the tumour arose from the ethmoid sinuses. Pain, nasal discharge and obstruction with facial asymmetry, and a nasal tumour were the commonest signs and symptoms; sanguineous discharge occurred in 8·5%, and ocular symptoms ultimately in 23%, while in 90% of cases there was clinical and radiographic evidence of bone erosion.

Treatment was with *x* rays and radium, alone or combined with surgery. Where the extent of spread was in doubt or surgical disfigurement inevitable, surgery was delayed until full irradiation had been given. *X* rays generated at 180 kV with 0·5 mm. copper or Thoraeus filter and 50 to 60 cm. F.S.D. were used through four fields extending from the eyebrow to the upper lip (see figure) to give a tumour dose of 6,000 to 7,000 r over 30 days. The eyes were protected with 3-mm. lead screens, though this was delayed on the side of the tumour until 1,000 r had been given. For intracavitary radium therapy four 50-mg. tubes filtered with 0·35 mm. of gold and 0·3 mm. of platinum and encased in 3 mm. of aluminium to increase distance were used. These were put into the cavity at the time of operation for from 3 to 5 hours, depending upon the dose of preoperative irradiation. Maxillary resection through the oral cavity was preceded by ligation of the homolateral external carotid artery. Up to 1945 operable cases were given small-dose preoperative *x* irradiation followed after 4 to 6 weeks by electrocoagulation combined with insertion of radium in the operation field. In 1946 and 1947 full-dose preoperative irradiation was given, but as no viable tumour could be found in a fair proportion of patients at operation, since 1948 operation has been reserved for post-irradiation recurrences.

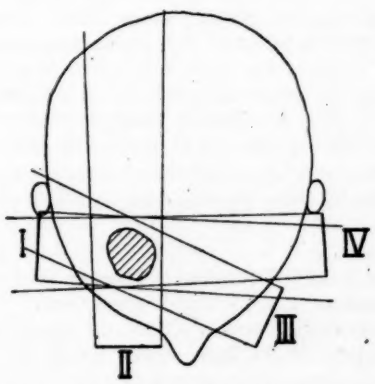

Diagram of a cross-section of the head illustrating the fields used.

The absolute 5-year cure rate was 23% and the relative rate 27%. After radiotherapy alone 12% of 142 patients, and after combined treatment 45% of 114 patients, survived this period. Lymph-node metastases were present initially in 10%, and ultimately in 23%, of cases

while in 10% metastases were generalized. The histological findings are analysed and related to metastasis, extent of involvement, and prognosis. It is concluded that involvement of the oral cavity is of bad prognostic significance. *G. E. Flatman*

273. **Improved Control of Advanced Oral Cancer with Massive Roentgen Therapy**
G. WHITE, J. SIENIEWICZ, and W. R. CHRISTENSEN. *Radiology* [*Radiology*] **63**, 37–42, July, 1954. 1 ref.

The authors have reviewed the results in 137 cases of advanced cancer of the mouth, including the tongue, tonsillar fossa, palate, and buccal mucosa, treated by radiotherapy at Pondville Hospital, Walpole, Massachusetts, between 1944 and 1951. In all cases there were advanced local lesions, and in many invasion of contiguous structures had occurred. Most of the cases were considered inoperable because of the site and stage of the disease, or because of the poor general condition of the patient.

Before 1947, a conventional tumour dose of 6,000 r was given, at 250 kV, 1·4 mm. Cu H.V.L. An attempt was made then to improve results by giving a massive tumour dose; the smallest dose given was 7,000 r and the largest 12,000 r, the average being about 9,300 r over a period of 3 to 4 weeks. This high dosage to the primary lesion was obtained largely by the use of an intra-oral cone covering as much of the diseased area as possible. Approximately half the total dose was delivered through the cone, and the rest through external ports. Treatment was begun with a daily dose of 400 r (in air) intra-orally, and 200 r through one of the external fields, since intrabuccal tolerance was reduced towards the end of treatment. Metastases in the cervical nodes were treated, after control of the primary tumour, by surgery or irradiation, or both.

With the earlier dosage (6,000 r) in only 6 out of 54 cases was the disease controlled at one year. After the institution of massive dosage, however, 40 out of 83 cases were under control at this period, and 23 remained well after 3 years. Radiation necrosis, immediate or delayed, occurred in 18 of the cases treated by massive dosage, and in only one of the cases treated with 6,000 r. So far as could be judged, a dose of 9,000 to 10,000 r appeared to give the best results; with doses above this level the incidence of radiation sequelae rose appreciably. Necrosis was treated by either conservative measures or by plastic surgery. *A. M. Jelliffe*

274. **The Value of Radiation Therapy in the Management of Intrinsic Tumors of the Spinal Cord**
E. H. WOOD, A. S. BERNE, and J. M. TAVERAS. *Radiology* [*Radiology*] **63**, 11–24, July, 1954. 4 figs., 18 refs.

The authors have analysed the results of irradiation in a series of 62 intrinsic tumours of the spinal cord treated at the Neurological Institute, New York. Of these, 23 were diagnosed only macroscopically at operation, but the remaining 39 were examined histologically and consisted of 23 ependymomata, 12 astrocytomata, 2 lipomata, 1 haemangioma, and 1 mesenchymoma. The average age of the patients was 37 years, and the sex distribution was even. Anatomically, the tumours arose from all parts of the cord, with the exception of the ependymomata, which were all located at the lower end. Treatment consisted of *x*-ray therapy (with technical factors of 200 kV, with 1 mm. Cu and 1 mm. Al added filtration) in varying dosage, which in most cases ranged from 1,500 to 2,000 r over 2 weeks, courses of treatment being repeated if indicated by clinical relapse.

No adequate control group, untreated by either surgery or radiotherapy, was available for comparison. However, the results of a previously reported series of 979 cases treated by surgery alone (Woltman *et al.*, *Arch. Neurol. Psychiat.*, 1951, **65**, 387) suggested that the average period of survival was 6 years. A 6-year survival rate was therefore adopted by the authors for purposes of comparison. On this basis 12 of 16 possible 6-year survivors amongst patients with ependymoma were alive at the end of this period. Corresponding figures were 5 out of 7 cases of astrocytoma, and 8 out of the 13 possible unclassified cases diagnosed only macroscopically at operation. Examination of the clinical records suggested that radiotherapy had led to arrest or reversal of the neurological changes in most cases. The authors discuss the difficulties encountered in treating tumours of the spinal cord, and suggest that surgery should be limited to taking a biopsy specimen and the drainage of any cysts that may be present. They advocate multiple short courses of radiotherapy rather than intensive treatment. *A. M. Jelliffe*

275. **Necrosis of Brain and Spinal Cord following *X*-ray Therapy**
N. MALAMUD, E. B. BOLDREY, W. K. WELCH, and E. J. FADELL. *Journal of Neurosurgery* [*J. Neurosurg.*] **11**, 353–362, July, 1954. 7 figs., 11 refs.

276. **Tuberose Sclerosis Treated by Deep Irradiation**
B. H. KIRMAN. *Journal of Mental Science* [*J. ment. Sci.*] **100**, 711–717, July, 1954. 5 figs., 19 refs.

277. **Fatal Post-radiation Pneumonitis**
A. G. W. WHITFIELD, R. LANNIGAN, and W. H. BOND. *Lancet* [*Lancet*] **2**, 117–119, July 17, 1954. 6 figs., 19 refs.

A case of fatal post-irradiation pneumonitis is fully reported by the authors from Queen Elizabeth Hospital, Birmingham. Attention is drawn to earlier reports of this condition in the literature, and it is stressed that, despite its rarity, it is important in that its differential diagnosis during life from pulmonary metastases, pulmonary infiltration by reticulosis, and pneumonia may be very difficult. Moreover, in addition to producing a severe illness, it may permanently lower pulmonary capacity and resistance to infection, and may even cause death.

The case reported is that of a man of 30 in a sedentary occupation who developed Hodgkin's disease of the neck, axillae, and mediastinum. The lung fields and abdomen were clear. He was given radiotherapy in the form of cervico-thoracic baths to a dose of 3,000 r in 26 days.

One month later he developed severe dyspnoea and cough and was found to have considerable limitation of inspiration. There was no evidence of extra-thoracic spread of the disease and the blood count was normal. Radiography showed shadows radiating from the hilum of both lungs. He was treated with oxygen, corticotrophin (ACTH), and cortisone, but rapidly deteriorated and died 72 hours after admission. At necropsy a litre of straw-coloured fluid was found in each pleural cavity, the lungs showed diffuse fibrosis but no evidence of Hodgkin's disease, and the treated lymph nodes showed dense fibrosis with scattered patches of surviving Hodgkin's disease.

The importance is stressed of bearing in mind the possibility that this complication may follow irradiation of the chest even when the dosage is not excessive.

R. D. S. Rhys-Lewis

278. **Treatment of the Resistant Stages of Hodgkin's Disease and Lymphoblastic Diseases**

A. HOCHMAN and M. ICKOWICZ. *British Journal of Radiology* [*Brit. J. Radiol.*] **27**, 467–468, Aug., 1954. 7 refs.

The histological changes produced by the action of *x* rays in lymphoid tissue are the same whether the tissue is itself irradiated or lies outside the direct beam. They appear, however, to involve adrenocortical activity, for after adrenalectomy the indirect effect of radiation is abolished while the direct effect is reduced. At the Rothschild–Hadassah University Hospital, Jerusalem, the authors have found that a much greater degree of lymphosis is produced by a dose of *x* rays or nitrogen mustard given after pretreatment with cortisone. These agents, even in small doses, reduce the cholesterol and ascorbic acid content of the adrenal glands, indicating that they act like stress in stimulating adrenocortical activity, and it is suggested that the diminution in effect of successive courses of treatment in lymphoblastic diseases may be due to adrenal exhaustion caused either by protracted illness or by the agents themselves. A therapeutic trial was therefore planned in which cortisone and nitrogen mustard were used together in the treatment of patients who had ceased to respond to nitrogen mustard alone.

Eleven patients, 7 with lymphadenoma, 2 with lymphosarcoma, one with reticulum-celled sarcoma, and one with giant follicular lymphoma, were studied, all of whom had advanced disease which had failed to respond to *x* rays and to nitrogen mustard. Cortisone was given in doses of 50 to 100 mg. a day by mouth, and had no noticeable effect when administered alone over a period of 8 to 10 days to 4 control patients. The dose of nitrogen mustard was kept low, 0·25 to 0·5 mg. per kg. body weight being given daily for 2 to 5 days. The most striking effect was the cessation of pain and fever, which occurred in all cases in which they were present. Shrinkage of large lymphoid masses also occurred in all cases, but in none was there complete subsidence. The improvement lasted only for one to 4 months however, thus precluding the practical application of this method, although the potentiating action of cortisone might be used earlier in the course of these diseases to obtain longer remissions with smaller doses of nitrogen mustard and possibly to delay the onset of resistance. Further experiments are in progress to determine the effects of nitrogen mustard on the indices of adrenocortical activity.

I. G. Williams

RADIODIAGNOSIS

279. **Prolapse of the Pyloric Antral Mucosa.** (Prolapsus de la muqueuse de l'antre pylorique, à travers l'orifice pylorique vers le bulbe duodénal)

A. YANNAKOPOULOS and G. VALAVANIS. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **43**, 505–522, May, 1954. 9 figs., 40 refs.

In a series of 806 barium-meal examinations 15 cases of prolapse of the mucosa of the pyloric antrum were found, all except 3 being in men. Ten cases are described in detail. The symptoms (such as epigastric fullness, belching, and acid reflux) are vague, but *x*-ray diagnosis is easy, and 9 radiographs showing the typical appearances are reproduced; two of them are stated to show a minute, definite or probable, prepyloric niche. [The association with duodenal ulcer is not mentioned, and none of the cases seem to have been confirmed pathologically.] Prolapse is the result of a combination of the functional state of the mucosa and hyperperistalsis. Hence it may be present during life, but not be seen at necropsy or in the operation specimen. On the other hand slight prolapse may be found after death without its necessarily having occurred during life.

[There is some doubt as to whether pyloric prolapse is in fact statistically associated with digestive symptoms. Even if it is, it is more likely to be the result of the functional disturbance than the cause.]

Denys Jennings

280. **Further Radiological Studies of the Movements of the Jejunum in Man, with Special Reference to Steatorrhoea**

G. M. ARDRAN, J. M. FRENCH, and J. W. MCLAREN. *Journal of the Faculty of Radiologists* [*J. Fac. Radiol. (Lond.)*] **5**, 267–275, April, 1954. 4 figs., 6 refs.

The authors' previous cinematographic studies of the movements of the duodenum and jejunum (McLaren *et al.*, *J. Fac. Radiol.* (*Lond.*), 1950, **2**, 148; *Abstracts of World Medicine*, 1951, **9**, 369) have now been repeated, using non-flocculating colloidal suspensions of barium sulphate. Direct serial films taken at a rate of 2 per second were again used, and motility was observed in 41 normal subjects, 17 patients with idiopathic steatorrhoea, and 7 patients with tropical sprue. No severe cases were included in this series.

A non-flocculating suspension is preferable to a simple suspension in saline in cases of steatorrhoea, as accurate examination is impossible if the barium is precipitated by mucus. To judge from the similarity of the two sets of films from normal subjects, alteration of the type of barium suspension had little effect in itself on intestinal

movements. In cases of steatorrhoea there seemed to be some diminution in the frequency of progressive segmentation as compared with normal subjects, and there was an increase in the calibre of the small intestine in many cases. No definite effects were seen after the administration of neostigmine or carbachol, but it is pointed out that the radiation hazard limited the period of observation to a maximum of 60 seconds; the method is thus less sensitive than balloon recording, which can be carried on for several hours. *Denys Jennings*

281. **The Radiological Diagnosis of Tumour of the Left Side of the Pancreas.** (Sur le diagnostic radiologique des tumeurs pancréatiques gauches)
L. MASSE and A. BARON. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **43**, 576–582, May, 1954. 4 figs., 12 refs.

Radiologically, a tumour of the tail of the pancreas produces a filling defect in the body of the stomach or in its greater or lesser curve or displacement of the vertical portion to the left. The importance of this last sign is emphasized. The condition differs radiologically from a gastric carcinoma in that the shape of the stomach changes with peristalsis and with change of position.
Denys Jennings

282. **Palpation of the Common Duct versus Peroperative Cholangiography in the Diagnosis of Common Duct Stones.** [In English]
S. BORGSTRÖM and O. NORMAN. *Acta chirurgica Scandinavica* [*Acta chir. scand.*] **108**, 13–24, Oct. 19, 1954. 2 figs., 22 refs.

283. **Transparietal Splenoportography.** (Spléno-portographie transpariétale)
G. F. LEROUX and A. DE SCOVILLE. *Journal belge de radiologie* [*J. belge Radiol.*] **37**, 89–138, 1954. 21 figs., bibliography.

Following experimentation on dogs, the authors, working at the Surgical Clinic, University of Liège, have employed transparietal splenoportography for the examination of 19 patients suffering from various diseases, including thrombophlebitis of the splenic vein, carcinoma of the pancreas and pyloro-duodenal region, and cirrhosis and metastases of the liver. The method is described. The examination appears to be without danger and hepatic tests have shown no alteration in liver function following it. In only one case did the spleen examined after splenectomy show evidence of an infarct caused by the puncture; this had given rise to no clinical symptoms. Blood in the peritoneum in quantities of 30 to 50 ml. was a usual finding, but in cases in which a large trochar had been used 100 to 150 ml. of blood was found; a needle of medium diameter should therefore be used. The puncture has not resulted in recurrence of haemorrhages in any case of hepatic cirrhosis.

It is pointed out that many serial films are necessary for the demonstration of the vascular pattern of the liver. The authors found the examination of great help in the cases they investigated, but believe it should be essentially a preoperative procedure. It is their belief that after further experience this method should prove of value in preventing useless operations such as resection of the stomach, colon, rectum, or uterus for carcinoma when metastases are already present in the liver.
John H. L. Conway-Hughes

284. **Pyelography after Direct Puncture of the Renal Pelvis.** [In English]
I. WICKBOM. *Acta radiologica* [*Acta radiol. (Stockh.)*] **41**, 505–512, June, 1954. 9 figs., 3 refs.

The author describes a new method of outlining the renal pelvi-caliceal system used by him at Sahlgrenska Sjukhuset, Gothenburg, Sweden, together with the results obtained in 5 cases, mostly of renal tumour. He claims that the method is of help in cases where there is deficient excretion of the contrast medium due to deficient renal function, or a poorly vascularized tumour where aortography has not given adequate information; furthermore, it is simpler to perform than retrograde pyelography, especially in males, and there is less danger of the spread of infection.

The technique is as follows. With the patient prone two calibrated metal markers are placed at right angles to each other on the skin of the back so that the crossing-point lies approximately over the renal pelvis. A similar marker is placed at the same level on the flank. Postero-anterior and lateral radiographs are taken, and by correlation of these the best point for puncture and an estimate of the depth of the pelvis are obtained. An injection of 10 ml. of "umbradil" is then made through a thin needle.

The procedure did not cause any discomfort to the patient, and no untoward results were found at subsequent operations apart from small haemorrhages in the perirenal fat. *W. B. D. Maile*

285. **Pyelographic Changes in Necrotizing Renal Papillitis**
B. WALL. *Journal of Urology* [*J. Urol. (Baltimore)*] **72**, 1–5, July, 1954. 3 figs., 20 refs.

In this paper from Barnes Hospital, St. Louis, and University Hospital, Augusta, Georgia, the author describes the radiological appearances in 3 cases of necrotizing renal papillitis associated with diabetes mellitus. He does not consider that the condition is uncommon, having found 100 cases in the literature, in 8 of which abnormalities were found on retrograde pyelography. The difficulty of differentiating these lesions from those of renal tuberculosis and chronic pyelonephritis is discussed, and details of the 3 cases are given. All 3 patients made a satisfactory recovery, the pyelogram being normal.

[The evidence in this paper is not sufficient to show that the radiological appearances indicate a specific entity; they could be those of a simple pyelonephritis occurring in a diabetic patient. Examination of the urine for acid-fast bacilli should usually permit differentiation of the condition from tuberculous infection.]
W. B. D. Maile

History of Medicine

286. **A Note on the Early History of Cerebral Localization**
B. STOOKEY. *Bulletin of the New York Academy of Medicine* [*Bull. N.Y. Acad. Med.*] **30**, 559–578, July, 1954. 4 figs., 23 refs.

Our knowledge of cerebral localization begins for many people only with the experiments of Fritz and Hitzig in 1870 and the researches of Ferrier in 1878, and has even been attributed chiefly to Broca. But in this paper the author points out that the groundwork was really laid in the preceding sixty years, and first and notably by the brilliant anatomical studies of Franz Joseph Gall (1758–1828) who was a German by birth, but studied at Vienna and Strasbourg and later assumed French nationality. However, had it not been for the persistent and continuing efforts of the French neurologist Jean Baptiste Bouillaud, Gall's work would have become submerged in the popular controversy over the new "science" of phrenology which was raging at that time. Gall, who had with Spurzheim been the first to demonstrate the crossing of the pyramidal fibres and so to explain how lesions on one side of the brain manifest themselves on the opposite side, and had also drawn attention to the function of the commissures, believed that the brain was exclusively the organ or centre of the moral and intellectual faculities and that each part of it subserved a particular function. Speech, he considered, was served by that part of the anterior lobe which rests on the roof of the orbit—a view which he supported by accounts of patients who had received injuries of the under surface of the frontal lobe and thereafter suffered from loss or defects of speech.

Bouillaud, who was born in 1796 and had been a pupil of Dupuytren and Magendie, confirmed the location of the centre for speech in the frontal lobe of the brain in studies which won for him election to the Académie de Médecine in 1826 at the early age of thirty. He placed not only speech but also the higher intellectual faculties in the frontal lobes, envisaged a "plurality of cerebral centres reserved for movement", and demonstrated that the cerebellum controls equilibrium; but general recognition was not accorded to his outstanding work, the prevailing concept that the brain acts as a whole being widely and stubbornly maintained. The matter rested there until 1861 when, at a meeting of the Anthropological Society of Paris, a great debate took place between Gratiolet—who held that the size and weight of the brain were the determining factors in intelligence and firmly expressed his adherence to the opinion that the brain acts as a whole—and Auburtin, pupil and son-in-law of Bouillaud, who supported his father-in-law's theory of localization.

The great Broca attended that meeting, and although inclined towards it, could not yet commit himself to the fundamental concept of a specific relationship of particular parts of the brain to particular functions. Five days later, however, the historic patient Leborgne, who had suffered loss of the faculty of speech for over 31 years, was transferred to Broca's clinic at the Hôpital Bicêtre; it was in this case that necropsy was later to show a cavity, the size of an egg and filled with fluid, in the posterior part of the second and third left frontal convolutions. By coincidence, in that same year Broca saw a further patient suffering from loss of speech, whose brain also showed a similar but more circumscribed lesion in the left hemisphere. Broca named this loss of articulate speech "aphemia", but the term was later changed by Trousseau to "aphasia". Trousseau, who was professor of clinical medicine at the Hôtel Dieu, had previously contributed nothing to the subject, but discarding Broca's term and substituting his own, he began in 1864 a series of lectures on the loss of articulate speech, while Bouillaud, who had laboured over the years (ably supported by Auburtin) to establish the principle of cerebral localization, lived to see the fruits of his labour taken away and his predominant position usurped by new-comers in the field. He referred to them contemptuously as mere "revisionists, organizers, subinventors, and correctors." Had it not been, however, for Auburtin's persistence in forcing the issue before the Anthropological Society, confirmation of the concept of cerebral localization might have been delayed still longer.

D. P. McDonald

287. **Acute Appendicitis. A Historical Survey**
J. A. SHEPHERD. *Lancet* [*Lancet*] **2**, 299–302, Aug. 14, 1954. 45 refs.

Observations of the pathological changes met with in the appendix were rare before 1800. In 1736 Amyand reported the removal of an appendix perforated by an encrusted pin and lying in a scrotal hernia. Mestivier (1759) is most often quoted as being the first to describe appendical inflammation. He found at necropsy on a patient who died after the opening of an abdominal abscess that the abscess was due to perforation of the appendix by a foreign body. Frequent reference to this case led to the view that acute appendicitis was often the result of foreign-body impaction. The first acceptable English account of perforative appendicitis was given by Parkinson in 1812; this is a report, without comment, of a case of general peritonitis following perforation of the appendix in a boy of 5. In 1824 Louyer-Villermay in France described 2 similar cases. About this time the French surgeon Dupuytren insisted that the *tumeurs phlegmoneuses* of the right side of the abdomen originated in disease of the caecum and denied the possibility of primary appendicular inflammation. Similarly German surgeons described perityphlitis, a vague caecal inflammation, as the cause of these right-sided abscesses, and maintained this view in spite of a paper in 1827 by Mélier

in which 6 further examples of appendicitis were described. For 50 years or more the acceptance of the hypothetical disease typhlitis as the cause of right-sided abscess hindered the advance of knowledge, though during this time many papers were published describing the true pathology of appendicitis, among them an article by Bright and Addison of Guy's Hospital in their *Practice of Medicine* (1839).

Hancock (1848) deserves credit for draining an appendical abscess before fluctuation had developed, thus defying current practice and saving the patient's life. In 1867 Willard Parker in the U.S.A. successfully drained four of these abscesses; this author recognized three stages in acute appendicitis—gangrene, perforated ulcer, and abscess. Mikulicz in 1884 first expounded the principles of surgical removal of the appendix, though it was Krönlein in 1886 who first performed laparotomy with the planned intention of removing the appendix. In one of his cases, although the appendicectomy was successful, the patient died; in another case with peritonitis, in which the appendix was not located, exploration and drainage saved the patient's life. In 1883 the British surgeon Symonds described an interesting extraperitoneal appendicectomy for a retrocaecal appendicitis with a palpable stone. Appendicectomy was carried out with success by several surgeons in the U.S.A., and Fitz in 1886 described the pathology of acute appendicitis and pointed out the need for early operation. By 1889 McBurney had operated on eight cases. Fowler (1894), Deaver (1898), and Murphy (1904) placed the subject in correct perspective.

In Great Britain progress was much slower. Treves, often credited with the first appendicectomy in this country, actually left the appendix behind after straightening it out. His insistence on what he called the "interval" operation delayed correct appreciation of the urgency of surgical intervention in these cases. In 1902 he did not remove the appendix of King Edward VII, but merely drained the abscess (no doubt rightly in this particular case). Treves lost his own daughter from a perforated appendix, no laparotomy having been performed.

A review of British literature does not enable credit to be given to any one surgeon for a planned appendicectomy, though Lawson Tait was probably among the first to carry out such a procedure. An "interval" appendicectomy was reported in 1890 by Lane from Guy's Hospital, London. It is all too clear that British surgeons were over-cautious in their attitude to appendicectomy. The author is of the opinion that this cautious approach may have been influenced by the fatal results of typhoid perforation, by the tendency for the physician rather than the surgeon to treat abdominal disease, and perhaps by Victorian stolidity.

J. G. Bonnin

288. **The English Diabetes (1674–1877)**
A. PATON. *St. Thomas's Hospital Gazette* [*St Thom. Hosp. Gaz.*] **52**, 189–191, Oct., 1954. 14 refs.

289. **Cholera in Quebec in 1849**
S. LEBLOND. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **71**, 288–296, Sept., 1954 12 refs.

290. **Guillaume-François Laënnec and Montpellier.** (Guillaume-François Laënnec et Montpellier)
L. DULIEU. *Scalpel* [*Scalpel* (*Brux.*)] **107**, 748–759, July 17, 1954. 7 refs.

Guillaume François Laënnec, born at Quimper in 1748, was the uncle of the more famous René Théophile Hyacinthe Laënnec. He studied medicine at the Universities of Paris and Montpellier, and practised at Nantes. His letters, edited by Alfred Rouxeau and published at Nantes in 1926, are the subject of the present paper, and are interesting for the light they throw not only on his own character, but on the state of medical education and qualification in France in the late 18th century.

Laënnec's observations, however, must be taken with considerable reserve, as he was clearly a young man who knew what he wanted and would tell any tale to get it. The fees for the examination for the doctorate of medicine at Paris were so excessive that most students went from there to other less expensive universities to qualify, and it had been agreed that Laënnec should go to Montpellier for this purpose. But his life in Paris was so pleasant that in a letter written to his father in April, 1771, every possible reason is advanced for postponing the move—the life at Montpellier was dissolute, the teaching was poor, and the time of year was unseasonable for a journey on foot. When it was suggested that he should go to Rheims instead, however, he appears from another letter, written in December, 1771, to have discovered unsuspected virtues in Montpellier, and the young student finally arrived there in October, 1772. Several vivid and doubtless exaggerated descriptions are given of life at Montpellier. There were a multitude of costly and formal degree ceremonies, extortionate fees were demanded by university servants, and repressive regulations were enforced by the authorities. Despite the conditions, Laënnec finally received his doctorate in March, 1773.

The last of Laënnec's letters quoted by the author (to which is added in an appendix a letter on the same subject written by a fellow Montpellier graduate, Pierre Blin, who was also practising in Nantes) reveals the confusion of authority which existed at that time, and which had brought him and other Nantes, practitioners into conflict with the Faculty of Nantes, who were trying to confine medical practice in Brittany to their own graduates. Laënnec and his friends refused to undergo the required examinations, and in this letter to Antoine Gouan, the professor of medicine at Montpellier, Laënnec describes the measures they were taking to defend the honour of the university which he had once decried. They finally took the matter to the courts, where they won their case and not only secured the right of Montpellier graduates to practise in the region, but also secured for them membership of the Nantes Faculty, of which Laënnec was elected Procureur Général 2 years later.

F. M. Sutherland

291. **Sir John Burdon Sanderson**
A. S. MACNALTY. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **47**, 754–758, Sept., 1954. 1 fig., 5 refs.